CONTENT SPECIFICITY IN IMAGINAL EXPOSURE: EVALUATION OF SUBJECTIVE AND PHYSIOLOGICAL RESPONDING IN PATIENTS WITH PANIC DISORDER

1996

MILLER

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
F. EDWARD HÉBERT SCHOOL OF MEDICINE
4301 JONES BRIDGE ROAD
BETHESDA, MARYLAND 20814-4799

GRADUATE EDUCATION OFFICE
(301) 295-3913
FAX: (301) 295-6772

TEACHING HOSPITALS
WALTER REED ARMY MEDICAL CENTER
NAVAL HOSPITAL, BETHESDA
MALCOLM GROW AIR FORCE MEDICAL CENTER
WILFORD HALL AIR FORCE MEDICAL CENTER

March 6, 1996

APPROVAL SHEET

Title of Thesis: "CONTENT SPECIFICITY IN IMAGINAL EXPOSURE: EVALUATION OF SUBJECTIVE AND PHYSIOLOGICAL RESPONDING IN PATIENTS WITH PANIC DISORDER"

Name of Candidate: Julie Kay Miller
Master of Science
Department of Medical and Clinical Psychology

Thesis and Abstract Approved:

J. E. Singer — 14 June '96

Jerome E. Singer, Ph.D. — Date
Chairman

N. Bradley Schmidt — 6/3/96

N. Bradley Schmidt, Ph.D. — Date
Member

Michael Feuerstein — 6/18/96

Michael Feuerstein, Ph.D. — Date
Member

The author hereby certifies that the use of any copyrighted material in the thesis entitled:

"Content Specificity in Imaginal Exposure: Evaluation of Subjective and Physiological Responding in Patients with Panic Disorder."

beyond brief excerpts is with the permission of the copyright owner, and will save and hold harmless the Uniformed Services University of the Health Sciences from any damage which may arise from such copyright violations.

Julie K. Miller
Department of Medical and Clinical Psychology
University Services University of the
Health Sciences

ABSTRACT

Title of Thesis: Content Specificity in Imaginal Exposure: Evaluation of Subjective and Physiological Responding in Patients with Panic Disorder.

Julie Kay Miller, Master of Science, 1996

Thesis directed by: N. Bradley Schmidt, Ph.D.
Assistant Professor
Department of Medical and Clinical Psychology

Although past research has suggested that imaginal exposure is effective in inducing arousal in both social and simple phobics, few studies have examined induction of panic in panic disorder patients via an imaginal paradigm. The present study examines the subjective and physiological effects of imaginal exposure via audiotaped vignette scenarios on patients panic disorder (PD) and normal controls (NC). Thirty-six subjects (20 PD, 16 NC) were exposed to a series of of four varied-content scenarios (3 threatening in content, 1 control). Subjective and physiological measurements were collected and compared to baseline. Content-specific responses were also examined to determine if PD subjects with identified specific content areas of threat would exhibit greater responding to content-congruent scenarios. This idea was partially supported, particularly with regard to Loss of Control and Social threat scenarios. As expected, PD subjects demonstrated greater responding. Twenty percent of the PD patients reported panic compared to only 4% of NCs. There were no group differences in physiological responding. Results support cognitive theories of panic and suggest that individuals with PD exhibit some situational specificity in perception of threat and precipitation of panic attacks.

CONTENT SPECIFICITY IN IMAGINAL EXPOSURE: EVALUATION OF SUBJECTIVE AND PHYSIOLOGICAL RESPONDING IN PATIENTS WITH PANIC DISORDER.

by

Lieutenant Julie Kay Miller

MASTER'S THESIS

Presented to the Faculty of the Department of Medical and Clinical Psychology
Uniformed Services University of the Health Sciences
in partial fulfillment of the requirements for the degree of
Master of Science 1996

TABLE OF CONTENTS

LIST OF TABLES

INTRODUCTION

Although Freud described panic attacks before 1900, no real attention was given to this form of anxiety until the past decade. During the 1980's the anxiety disorders became a more central focus of interest in mental health. The 1984 overview of psychiatric progress in the Journal of the American Medical Association was largely devoted to anxiety disorders, and related symptomatology; particularly Panic Disorder, agoraphobia, and panic attacks (Freedman and Glass, 1984). Numerous journals have published special supplements on the topic, and each successive edition of the Diagnostic and Statistic Manual of the American Psychiatric Association (APA) places greater emphasis on the role of panic attacks in the classification and etiology of anxiety disorders (APA, 1984; APA, 1987; APA, 1994)

The Definition of Panic

The technical definition of a panic attack involves what appears to be a reliance on the experience of four of the following symptoms (from a possible 13): 1) palpitations, pounding heart, or accelerated heart rate; 2) sweating; 3) trembling or shaking; 4) sensations of shortness of breath or smothering; 5) feeling of choking; 6) chest pain or discomfort; 7) nausea or abdominal distress; 8) feeling dizzy, unsteady, lightheaded, or faint; 9) derealization (feelings of unreality) or depersonalization (being detached from oneself); 10) fear of losing control or going crazy; 11) fear of dying; 12) paresthesias (numbness or tingling sensations);

13) chills or hot flushes.

BACKGROUND

THEORETICAL MODELS

Biological Models of Panic

The popular biological models of panic have had major consequences for the conceptualization and treatment of panic disorder and agoraphobia. Biological investigators have posited various neurobiological sources of PD (Carr & Sheehan, 1984; Klein, 1981; Sheehan, 1982a). Several researchers propose a qualitative biological distinction between PAs and other forms of anxiety. The primary areas of argument for their models include drug specificity, panic induction, spontaneity of PAs, genetic data, and separation anxiety (Klein, 1981). The major impetus for this biologically-focused emphasis has stemmed from Klein's early work. Klein posits a basic distinction between panic attacks and other types of anxiety. In the 1980's. Klein and his colleagues noted that patients suffering from recurrent "attack-like" anxiety responded therapeutically to administration of tricyclic antidepressants (Klein and Fink, 1962; Klein, 196-; Mendel and Klein, 1969). Subsequently Klein formulated a new theory of pathological anxiety (i.e., Klein, 1980, 1981) based upon a qualitative distinction between what he called panic anxiety, and chronic or anticipatory anxiety. Panic anxiety is characterized by an acute,"attack-like" course of a specific group of primarily somatically-based symptoms. In Klein's model, panic attacks often occur spontaneously, "out of the blue". These symptoms represent a specific biological dysfunction. In contrast, anticipatory anxiety is

triggered by specific stimuli (or the anticipation of them), and therefore usually occurs in feared situations or during anticipation of such situations. Anticipatory anxiety has a more chronic, unremitting course, fewer fluctuations and more cognitively-focused symptoms.

Within Klein's framework, and its qualitative distinction between panic and anticipatory anxiety, the chronic anxiety and avoidance of the agoraphobic patient is seen as the learned consequences of experiencing spontaneous panic attacks. What the patient fears most is the recurrence of the attacks versus the associated milieu. This view is similar to several other authors who have conceptualized PD as "fear of fear" or "phobo-phobia" (i.e., Westphal, 1871; Frankl, 1975; Beck and Emery, 1979; Chambless, 1982; Griez and van den Hout, 1983). Conversely, however, these researchers are among many who assume a quantitative rather than a qualitative difference between panic and anxiety (i.e., Lader, 1982; Mefferd, 1979).

Klein, drawing from his earlier theory, relates panic attacks as analogous to an adult separation anxiety response (Klein, 1981). He outlines an innate mechanism in animals and humans that is activated by separation from attachment stimuli. This in-born alarm mechanism consists of a protest and a despair component, viewed by Klein as parallel to Bowlby's (1969, 1973) first two stages of the separation anxiety response. The protest component of the alarm mechanism includes the elicitation of panic, including active, help-seeking behavior; and the despair component includes the elicitation of depression. Klein maintains that this alarm mechanism is activated by minimal triggers or without triggers because the threshold for alarm is chronically lowered in such individuals. This leads him to speculate that "the sole function of all antidepressants is simply to raise

thresholds throughout this apparatus... and that their beneficial effects on anxiety attacks and/or depression result from this normalization of reaction" (Klein, 1981, p. 248). His concept of alarm activation does not specify the conditions determining whether panic or depression will predominate.

Klein's model is consistent with the approach advocated by much of the biologically-based psychiatric research on anxiety. Sheehan, for example, also argues for a biological explanation for panic disorder (Sheehan, 1982a, b; Carr and Sheehan, 1984). Sheehan divides pathological anxiety into specific "endogenous" and "exogenous" subtypes, similar to the delineation commonly proscribed to depression (Sheehan and Sheehan, 1982a, b, 1983; Sheehan, 1984). Endogenous anxiety is outlined by the presence of "spontaneous" panic attacks and is a "metabolic disease" (Sheehan and Sheehan, 1983; Carr and Sheehan, 1984). According to Sheehan's model, the patient first experiences a "subpanic symptom stage" with panic symptoms occuring for no identifiable reason. Later, the first "full blown panic attacks" occur with anxiety symptoms and a desire to flee. In the next stage, the patient is increasingly hypochondriacal and preoccupied with the search for the cause of the attacks. Derealization and depersonalization are common in this stage. Subsequently, simple and social phobias can develop and be manifested as panic attacks in specific situations (classical conditioning). At this point, the patient may increasingly restrict his or her lifestyle to such a marked degree that a reactive depression develops.

Status of Empirical Support for the Biological Models

Despite the heuristic value of these popular biological models, the empirical basis for many of the major assumptions and postulates is tenuous. A solely biological model

appears unable to integrate many of the relevant findings, and the lack of empirical evidence to support many of Klein's foundational arguments is impressive.

Fundamental Assumptions

First, the most fundamental and strongest assumption in Klein's theory, the drug-specificity argument, is not supported by the majority of empirically-sound drug treatment studies. This argument, which has posited that benzodiazepines should be ineffective in treating panic-related anxiety, has been refuted in studies which document the efficacy of alprazolam and diazepam, in the treatment of panic (Chouinard, Annable, Fontaine, and Solyom, 1982; Shader, Goodman, and Gever, 1982; Marks, 1983; Noyes et al., 1984). Furthermore, the additional assumption made within the drug-specificity argument, that antidepressants are not effective in treating anticipatory anxiety is tenuous at best. Other researchers have proposed alternate plausible explanations for the efficacy of antidepressants in panic attacks which contradict Klein's "direct blockade" assumption. For example, Marks (1983) proposes a depression-mediation mechanism whereby antidepressants alleviate depressive symptoms, which has the secondary effect of reducing the occurrence of PAs; while Telch et. al. (1985) offer an exposure-facilitation mechanism in which antidepressants facilitate exposure to feared situations, resulting in reduced panic frequency.

Second, Klein cites the ability to experimentally induce panic in panickers, but not normal controls, using a biological challenge agent, as evidence of the power of the biological theory. Not only is the interpretation of such findings as support for the biological model questionable in itself, the numerous methodological problems, including

lack of consideration of cognitive variables and inadequate control of expectancy bias in Klein's study made such interpretations empirically unsound (Margraf, Ehlers, and Roth, 1986a). Furthermore, without the consideration of cognitive and perceptual variables, such results, even if valid, would not inform us as to whether such findings are actually the result of cognitively-based differences in the appraisal and interpretation of the stimuli. So, even if greater numbers of panic patients versus controls do panic when exposed to such stimuli, one cannot assume the reason is biologically-based if possibilities that panickers may be appraising stimuli differently (e.g., as more intense or unpleasant), or interpreting their significance or effect differently (e.g, as harmful, catasrophic in effects) have not been considered. In short, the panic-induction studies provide little basis for Klein's or Sheehan's models.

Third, the claim that the majority of panic attacks occur spontaneously, without identifiable cues or triggers, is another claim that proponents of the biological model believe buttresses their theory. It is true that a proportion of PA's seem to be unanticipated in many patients (Taylor, Telch, and Havvik, 1983; Margraf et. al, 1986a). However, the idea that the apparent spontaneity of some PA's represents an autonomically-linked biological dysfunction that is without psychological, perceptual, or environmental influence is merely an assumption that has not been empirically demonstrated.

It is clear that precipitating events operating during the first days or hours may be important in the occurence of PAs (Brehony and Geller, 1981; Mathews, Gelder, and Johnston, 1981; Raskin et. al., 1982). These precipitants can be a feared situation or

anticipation of a feared situation, or non-specific stress. When panic attacks occur in fixed situations, they can be said to be spontaneous only in that their exact time of occurrence within the larger time frame or context cannot be predicted. Yet central to the validity of current biological models of panic attacks is whether immediate external or internal triggers for individual panic attacks exist. If such triggers are regularly present, the distinction between 'spontaneous' panic (as defined above) and cued anxiety is invalidated. The most promising candidates for such triggering events are either bodily sensations interpreted as dangerous or anxiety-inducing thoughts. Hibbert (1984) found specific cognitions preceding or simultaneously occuring with panic attacks or anxiety in all investigated patients. The panic patients' cognitions were more intrusive, more centered on death, illness, or loss when compared with cognitions of non-panickers. Similar findings have been elicited in studies by Finlay-Jones and Brown (1981) and Ley (1986). So, although the question of spontaneity of panic attacks has oniy recently begun to be studied carefully, the existing evidence implies internal cues immediately triggering individual panic attacks versus "spontaneous panic"(Hibbert, 1984; Beck and Rush, 1985; Ley, 1985).

Furthermore, numerous studies have shown quite conclusively that a variety of psychologically and as well as physiologically stressful events may contribute to the onset or frequency of panic symptoms (Klein, 1964; Finlay-Jones and Brown, 1981; Brehony and Geller, 1981; Tearnan, Telch and Keefe, 1984). In fact, even in studies interpreted to bolster the biological view (e.g., Klein, 1964), events that are interpreted as physiological stressors (i.e., menopause) have obviously powerful potential psychological effects as

well. Although there is some question as to whether some internal or external trigger exists for all episodes of panic, Klein interprets the lack of an obvious external trigger as evidence in support of the biological model. This assumption, based entirely upon clinical impressions, appears unrealistic. It seems ungrounded to expect such triggers or cues to be obvious or consistent across individuals. Just as individuals vary biologically, they vary experientially and cognitively in how they perceive stimuli. Thus, it is not surprising that evidence has been found for a gamut of internal and external triggers, which, depending upon their cognitive interpretation, may precipitate panic-like symptoms (Hibbert, 1984; Beck and Rush, 1985; Ley, 1985).

Klein's remaining two arguments for the biological camp are what he interprets as supportive data regarding genetic factors and the role of separation anxiety in the development of panic. The data on both of these questions is less abundant, and less conclusive. Although there is evidence for some influence of genetic factors from twin studies, even these researchers admit that the results vary greatly depending upon the various criteria used to assess psychiatric symptoms (Carey and Gottesman, 1981). Furthermore, some findings which support increased familial risk may be attributable to sampling error (Carey and Gottesman, 1981; Torgersen, 1983). Unfortunately, there are very few methodologically-sound adoption studies to clarify this issue, and the high rate of non-concordance among monozygotic twins, and unaffected first-degree relatives demonstrates the significant influence of environmental factors (Carey and Gottesman, 1981; Torgersen, 1983). Thus, the genetic transmission of panic-proneness independent of generalized anxiety has yet to be demonstrated.

Finally, Klein's idea that separation anxiety in childhoood represents the same mechanism that precipitates adult panic is based upon his own empirically-flawed studies (Klein, 1964; Klein, Zitrin, Woerner, and Ross, 1983; Gittelman-Klein and Klein, 1984). These studies each had a variety of potential flaws, including absence of control groups, lack of standardization, and retrospective design. Other more methodologically-sound (but still retrospective) studies have contradicted Klein's findings of increased levels of childhood separation anxiety histories in adult panic patients (Berg, Butler, and Pritchard, 1974; Solyom, Beck, Solyom and Hugel, 1974; Raskin, Peeke, Dickman, and Pinsker, 1982). So, the relationship between childhood separation anxiety and adult panic attacks is tenuous, possibly due to the purely retrospective nature of the studies conducted up to this point. Thus, despite the heuristic value of their models, alternative approaches focusing on the interaction of physiological and psychological factors seem more capable of integrating the relevant findings.

Biological Challenges

As a result of the proliferation of the biologically-based models, biological challenge manipulations are the most frequently-used experimental paradigms for investigating the neurophysiological bases of panic disorder. Such paradigms stem from the hypothesis that specific biochemical agents (i.e., sodium lactate, CO_2, caffeine, yohimbine, isoproterenol, cholecystokinin) precipitate panic by triggering a neurochemical dysregulatory mechanism, subsequently eliciting excessive autonomic arousal. Athough this basic principle has been well-supported by research which shows that PD subjects show significant increases in anxiety levels after infusion of sodium lactate (Liebowitz et al., 1985; den Boer,

Westenberg, Klompmakers, and Van Lint, 1989; Yeragani et al., 1987) or exposure to other biological challenge agents, the response of PD patients to such challenges does not negate the effects of cognitive variables.

For example, Margraf, Ehlers, et al., (1986b) elucidated numerous significant methodological flaws in studies of sodium lactate infusion that limit the ability to conclude, as Klein and Sheehan did, that sodium lactate is an inducer of panic almost exclusively in panic patients (Klein, 1981; Carr and Sheehan, 1984). In fact, Ehlers et al. (1986), found that lactate infusions induced subjective physiological arousal similarly in panickers and normals. None of the biological mechanisms seems to explain the effects of lactate infusions or CO_2 inhalations adequately. A more comprehensive model that includes the internal physiological changes, environmental cues, and, individual appraisal of this information as dangerous would be more promising. Only by including such cognitively-loaded variables will such a model be complete. If such variables are excluded, one has no way of validly determining whether reported or observed physiological variations are due to biological differences or cognitive ones. Clearly, if cognitive and perceptual variables were not important, they would not be included in the DSM-IV criteria; indeed, the inclusion of PAs and PD within the manual of "mental disorders" would not even be appropriate. Inclusion of these variables is vital, and it is only through such specific knowledge grounded in a complete model that the most efficacious treatments and/or cures will have the solid base from which they may be properly developed.

Psychological Models of Panic

There has long existed an understanding that psychological factors may play an important role in panic disorder. Since the end of the nineteenth century to the publication of the DSM-IV in 1994, panic disorder has been subsumed under a variety of pseudonyms, many implying this "mental" involvement. These diagnoses included anxiety neurosis, effort syndrome, neurocirculatory asthenia, cardiac neurosis, soldiers' heart, and irritable heart (e.g., Soley and Shock, 1938; Cohen and White, 1950).

Lang's bioinformational porcessing theory (1979) postulates that affective states and their physiological, behavioral, and cognitive asssociations, including external cues, may be elicited via re-creation of appropriate imagery. He posits that during emotionally-charged situations (including PAs), physiological responses, behavioral responses, situational cues, and associated meanings, are encoded and stored in memory associations. Thus, in applying this theory to anxiety states, anxious affective states may be elicited merely by thinking about information associated with the anxiety. These thoughts alone may produce physiological fear symptoms analogous to the related affective state, since the information is associated with anxiety. Thus, the recollection of information associated with anxiety should elicit the signs and symptoms of emotional fear.

Recently, there has been an increase in research into the understanding of psychological factors involved in the maintenance of panic disorder and panic attacks. Description of PAs as recognizable fear reactions to identifiable triggers has provided a basis for panic

disorder that is more like that of the other anxiety disorders (e.g., phobias). Thus, models of panic disorder now share many similarities with models of other anxiety disorders, including the important role of cognitions and interpretation of stimuli.. Most noted of these authors have been Goldstein and Chambless (1978) who posited that PD symptoms are characterized by a "fear of fear" with somatic symptoms occuring during panic attacks often interpreted as signs of impending catastrophe. In a similar fashion, Beck and Rush (1975) focus upon the importance of cognitions concerning the anticipation of danger in anxiety attacks, particularly physical survival concerns like death.

Beginning in the 1980's, some increasingly specific psychological models of panic disorder evolved. These models began to focus on more specific psychological mechanisms not just in influencing cognitions during a PA, but in the actual precipitation of PAs (e.g., Beck, Emery, and Greenberg, 1985; Clark, 1986; Beck, 1988). These models offered the alternative explanation for panic; panic actually results from catastrophic misinterpretation of challenge-induced bodily sensations, or cues. The perception of bodily cues, a process known as interoception, is a necessary component which may act as a primary trigger in psychological models of panic. Previous clinical observations by Beck and Emery (1979), and Beck, Emery, and Greenberg (1985) suggested that panic attacks involve a perturbation in an individual's physiological state which leads to interpretation that these physiological sensations indicate a serious physical disorder. This, in turn, causes the individual to experience extreme anxiety. Although this description closely resembles other models of panic disorder, Beck et al. (1985) did not restrict their theory solely to concerns about internal events. They suggested panic attacks

could involve external triggers as well. Thus, these authors appear to equate panic disorder with any heightened anxiety rather than limiting themselves to the DSM-IV definition.

Clark's cognitive approach (1986), suggests that panic attacks are caused by a misinterpretation of bodily sensations as being dangerous. This association of bodily symptoms with specific dramatic outcomes is a critical feature of most of the psychological models of panic. Specifically, Clark proposed that an initial stimulus (internal or external) results in some type of perception of threat, which leads to apprehension. Subsequently, the apprehension leads to bodily sensations that are misinterpreted (or misassociated) in a catastrophic fashion leading to even greater perceived threat, and so on.). Theoretically, the bodily sensations can come from a gamut of occurences, including other emotional states, caffeine, exercise, rapid movement, etc. (Clark, 1986). In accordance with these views, Salkovskis and Clark (1990) argued that the wide variety of biochemical panic provoking agents produce panic via their ability to generate misinterpretable physical sensations rather than through specific biochemical pathways.

Status of Empirical Support for the Psychological Models

The idea that affective states and their interpretation may be influenced or modified by the cognitive associations attached to them is not new. As early as the 1960's, Schacter and Singer's (1962) landmark study showed that individuals who are aroused (emotionally and physically) appraise the context of such arousal before cognitively

labeling the arousal (e.g., fear, excitement). It is therefore no surprise that similar mechanisms may operate in the extreme arousal state of panic as well.

Overall, psychological models have received support from several investigations suggesting cognitive factors play a crucial role in moderating the PD subjects' panic response. Salkovskis and Clark (1990) manipulated subjects' tendency to interpret hyperventilation-induced sensations as either positive (good psychological adjustment) or negative (risk for fainting). Subjects in the positive interpretation group experienced hyperventilation as pleasant, while subjects in the negative interpretation group viewed the hyperventilation as unpleasant. Several studies have shown that cognitive factors affect subjects' emotional responses to CO_2 inhalation (Rapee, Mattick, and Murrell, 1986; Telch and Harrington, 1993; van den Hout and Griez, 1982). For instance, van den Hout and Griez informed normal subjects that CO_2/O_2 inhalation would produce either tension or relaxation. Those given tension instructions reported an increase in tension sensations, while those in the relaxation condition reported an increase in relaxation sensations.

Somatic Sensations and Associations

Regardless of the specific model, one prediction from psychological theories of PD is that patients with PD should be more likely to panic when exposed to various somatic sensations. Indeed, there is an amassing collection of empirical literature demonstrating that PD patients are more likely to report anxiety or panic in response to a wide variety of manipulations (so-called "biological challenge tests"), which have as their main source of commonality the ability to produce a range of bodily sensations commonly found in panic attacks (i.e.., Barlow, 1988; van den Hout, 1988; Rapee, 1990).

Additionally, there is some evidence that PD patients are more likely to report greater anxiety than other patients or normal controls in response to bodily sensations produced by a number of common sensation-producing experiences such as aerobic exercise, rapid rotation, or breathing through a narrow straw (Zarate, Rapee, and Barlow, 1989). Finally, one study has demonstrated that panic disorder patients also report excessive anxiety in response to manipulation-induced perceptions of increased heart rate through false heart rate feedback (Ehlers, Margraf, Roth, Taylor, and Birbaumer, 1988). Although the experimental paradigms differ, they share the specific focus on the perception and interpretation of somatic sensations.

The important role of associations was again demonstrated in Rapee et al.'s (1992) study which compared the effects of inhalations of 5.5% carbon dioxide in air and 90 seconds of voluntary hyperventilation in subjects with several anxiety-related DSM-III-R diagnoses, as well as normal controls. Findings indicated that subjects with panic disorder reported a greater number of physical and cognitive symptoms, more fear, and more catastrophic cognitions in response to both challenges. It is significant to note, however, that fear levels, even for the panic disorder subjects, were not particularly high and not all PD subjects reported experiencing a panic attack (47% hyperventilation; 65% carbon dioxide). This is consistent with results of other biological challenge studies. Thus, simply experiencing somatic sensations is not sufficient to trigger panic in PD patients. In point, psychological theories of PD predict that somatic sensations must be associated with dramatic (negative or catastrophic) outcomes in order to result in panic. In addition, while PD patients are more likely to have such associations than others, this will not occur

at all times or in every situations. Thus, determination of the factors that may influence response to biological challenge procedures could provide additional evidence for the success of psychological models to predict PD.

As previously described, PD patients are more likely than other subjects to report thoughts of dramatic (negative and/or catastrophic) outcomes following detection of somatic sensations (Chambless and Gracely, 1989; Rapee, 1985). In Chambless and Gracely's study of 271 outpatients with various anxiety-based diagnoses (as well as those with depresssion), PD patients (and those with agoraphobia), scored significantly higher scores on items describing thoughts that physical illness would develop as a result of their anxiety. The Agoraphobic Cognitions Questionnaire (ACQ) and Body Sensations Questionniare (BSQ) were used.

In addition, some studies have found that a specific set of somatic sensations appear to be especially noted by PD patients (Anderson, Noyes, and Crowe, 1984; Barlow et al., 1985; Rapee, Sanderson, McCauley, & Di Nardo, 1992). These symptoms are generally those that have to do with the autonomic, cardiovascular, or respiratory systems and could be considered to be "more serious" anxiety symptoms. In Anderson et. al's family study, patients with PD and GAD were compared on their patterns of symptoms, age, onset characteristics, personality characterisitics, course of illness, and outcome. Subjects with PD were shown to report more somatic (particularly autonomic) symptoms over their course of illness, and a later, more abrupt onset of illness compared to those with GAD. In particular, cardiovascular symtpoms such as palpitations, chest pain, and dyspnea) were reported by the majority of the patients with PD, but were rarely reported by GAD

patients. Barlow et. al's study of panic resulted in similar findings in 108 anxiety-disordered patients. This study also found that patients with PD (both those with and without agoraphobia) reported significantly more of the largely somatic symptoms (including dyspnea, palpitations, chest pain, shakes) than patients with other anxiety-related diagnoses, depression, or cued panic.

In a more detailed investigation of self-reported associations, McNally and Foa (1987) found that untreated subjects with PD and agoraphobia rated arousal-related events (somatic symptoms) as more likely and more threatening than did normal controls or agoraphobics who had been successfully treated. This difference was not found for non-arousal unpleasant events. Additionally, untreated agoraphobics were more likely to provide a threat explanation for ambiguous internal or external events than the other groups.

In a similar study, four types of ambiguous events were described to PD patients, other anxiety disorders, and normal controls (Clark et al., 1988). The four types of ambiguous situations were sudden bodily sensations (i.e., "your heart is beating quickly"), social situations, general external events, and long-term bodily events (i.e., "a small spot on the back of your hand"). While panic patients tended to report more threatening interpretations in response to all of the scenarios, the major and most notable difference was for sudden bodily sensations. In addition, PD patients showed a significant decrease in their tendency to engage in threatening interpretations of these bodily sensations following successful treatment (Clark et al., 1988). These findings seem to imply that PD

patients may indeed have a natural inclination toward negative, catastrophic interpretation of stimuli, particularly, somatic sensations.

Examination of associations between somatic sensations and threat has also come from self report measures of these associations. One instrument which has received a great deal of attention has been the Anxiety Sensitivity Index (Reiss, Peterson, Gursky, and McNally, 1986). The ASI is a 15-item scale that assesses fear of somatic sensations (e.g., "it scares me when my heart pounds"). Interestingly, early research has found that scores on the ASI are distributed normally in the general population suggesting that fear of somatic sensations is a common, dimensional construct. Consistent with psychological models of panic, patients with PD score higher on this construct than those with other anxiety disorders or normal controls.

An obvious prediction from the psychological models of PD is that such individuals allocate excessive attentional resources to the detection of somatic sensations, and/or to task which deal with subject matter relevant to those sensations.

Numerous studies have shown that anxiety patients respond selectively to the perception of verbal somatic threat cues (Mathews and MacLeod, 1985; MacLeod, Mathews and Tata, 1986; Mathews and MacLeod, 1986). These studies demonstrate that selective attention towards threat cues can occur long before the individual is aware of the stimulus material. If the same holds true with panic, selective attention allocation towards physiological changes might start the positive feedback loop at a very early stage

A study by Clark et. al. (1988) compared PD patients with non-anxious controls on their reaction time to naming the last word of a sentence. Several of the ambiguous

sentences involved somatic sensations, (e.g., "If I had palpitations I could be..") were presented on a computer screen; this sentence was then replaced with a single word and subjects were instructed to read that word aloud as quickly as possible. This word could either be a threat word (e.g., dying) or a neutral or pleasant word (e.g., excited). Panic patients were significantly faster at reading the threat words than the neutral words while normal controls did not differ. This study provides evidence for the stronger association between somatic sensations and threat in PD patients than normal controls.

Similarly, Ehlers et al. (1988), via use of a modified Stroop color-naming task showed that PD patients and occasional panickers have great performance disruptions than normals by physical threat words. Similarly, Hope et al. (1990) demonstrated that social phobics are more disrupted by social threat words, while panickers are more disrupted by physical threat words.

Another popular hypothesis is that panic patients are particularly keen in perceiving bodily symptomatology. Psychological models suggest that panic patients may allocate excessive attentional resources to their internal sensations. Thus, when bodily sensations occur, panickers should notice them more easily and earlier than others. Evidence on this has been mixed. In one study which required subjects to match their heartbeat to the beat of a metronome, Ehlers et al. (1988) found no evidence for improved heart rate perception in panic disorder patients. This finding was supported in a similar study which found no relationship between accuracy of heart rate estimation and scores on the ASI in normal subjects (Butler and Rapee, 1991). However, in Ehlers and Breuer's (1992) later study using different methodology (subjects estimated the number of heartbeats in a given time

period), PD subjects were more accurate in estimating their heart rate than normal controls. Another study which used this method found that PD subjects were more accurate in estimating heart rate than normal controls but showed no difference in heart rate estimation when compared with social phobics (Antony et al., 1990).

Another study (Ehlers, 1995) involved detection of a vibration given to the patient's finger that was either paired or not paired with a mild electric shock. Subjects with panic attacks were faster at detecting the vibration when it was paired with shock than were non-anxious controls. Although the existing models do not necessarily predict that when subjects are instructed to scan their bodies, panic patients will be more accurate at identifying sensations, such a finding would certainly enhance psychological models and clearly requires further investigation.

Cognitive Manipulations

A number of studies have utilized various cognitive manipulations to ascertain their effect on the response to biological challenge procedures. Some of these manipulations have included expectancy of threat (Margraf, Ehlers, and Roth, 1989; Salkovskis and Clark, 1989; van der Molen, van den Hout, Vroemen, Lousberg, and Grie: 1986), attributions of threat (Kenardy, Evans, and Oei, 1988; Rapee, Mattick, and Murrell, 1986, perceived control (Sanderson, Rapee, and Barlow, 1989), and perception of safety (Rapee, Telfer, and Barlow, 1991). Overall, Rapee (1990) suggested that the two broad psychological constructs that have the most support for their influence on biological challenge procedures are associations of somatic sensations with threat and perceived control over threat.

Perceived Safety

The effect of safety cues and the resultant increased perception of safety is one specific variable that has been examined as a psychological moderator of subject responses to sensation-inducing stimuli. These cues are believed to ameliorate anxiety levels in response to a stimulus by providing information that suggests that the stimulus or the threatening component of the stimulus, will not occur.

Two of the most impressive demonstrations of the importance of various psychological variables (e.g., safety information and safety cues) are those by Rapee et al. (1986) and Sanderson et al., (1989). In the former, PD patients and social phobics were assigned to one of two conditions, an information group and a no-information group, and given single breath inhalations of 50% carbon dioxide and 50% oxygen. Subjects in the information group were given complete and explicit information about the effects and harmless nature of the inhalation. Subjects in the no-information group were given minimal information about the inhalation, thus allowing them to engage in their usual associations. PD patients but not social phobics in the no-information group reported a much more dramatic response to the inhalation than subjects in the information group.

Recently, another interesting study examined the effects of having a safe person (as a safety cue) present during a carbon dioxide inhalation challenge. Panic patients without a safe person present reported greater levels of distress, more catastrophic cognitions, and greater levels of physiological arousal than panickers who had a safe person present (Carter, Hollon, Carson, and Shelton, 1995).

Perceived Control

Perceived control appears to be another important moderator of panic and anxiety (Barlow, 1988). Sanderson, Rapee, and Barlow (1989) found that panic patients who falsely believed they could regulate CO_2/O_2 levels during a biological challenge task were less likely to panic compared to patients who believed they had no control over inhaled CO_2/O_2 levels (Sanderson, Rapee, and Barlow, 1989). In addition, not only were the subjects who believed they had no control more likely to panic, but their number of panic symptoms and catastrophic cognitions was greater, as well as their levels of reported subjective anxiety and panic.

Mental Imagery

Powerful additional support for cognitively-based mechanisms of panic was recently introduced by studies which have demonstrated mental imagery-induced physiological and subjective distress in the laboratory (Watkins et al., 1990). The few studies that have addressed this specific area suggest that catastrophic attributions regarding the source and meaning of panic symptoms are vital for the successful induction of panic via experimental manipulation. Watkins et al. (1990) examined subjective and somatic arousal in PD subjects using neutral, relaxation, stress, and panic imagery. Subjects exhibited significant elevations only in response to stress and panic focused imagery which included suggestive prompts within the imagery descriptions, such as physiological and cognitive reactions, and description of the environment. So, although the precipitating stimuli associated with panic attacks may be more complex (and thus more difficult to manipulate), PD subjects

should respond to imaginal exposure when exposed to a meticulously designed paradigm which incorporates negatively-focused cognitive propositions, such as catastrophic meaning elements, within the imaginal scenes. Watkins et. al's study was unique in this inclusion of cognitive propositions within the imaginal scenarios. If PD patients possess an inherently restrictive, negatively-focused cognitive schema through which they interpret imagery or physiologically-based symptoms, then they should exhibit higher levels of fearful responding and catastrophic cognitions when given the same information and stimuli as normals. In sum, Watkins et. al's findings support this idea.

Although a few studies (e.g., Lang, Levin, Miller, and Kozak, 1983) have examined physiological differences in responding for subjects pre-trained for an internal (bodily sensations) or external (situational cues) focus conditions, even fewer have analyzed physiological and/or psychological changes in response to imagery (Levin, Cook and Lang, 1982; Cook, Melamed, Cuthbert, McNeil and Lang, 1988; Watkins et al., 1990). Lang et al.'s (1983) study showed that subjects pre-trained for an external focus content in the imagery stimuli failed to exhibit significant somatic (including heartrate) changes. While Watkins et al. (1990) did find significant heartrate changes with their inclusion of cognitive propositions within the stress and panic scenes, they concede such findings are tentative since they did not have a comparison group without prompts. McNeil, Melamed, Cuthbert, and Lang's (1983) study found that simple phobics, and to a lesser degree, agoraphobics, showed significant heartrate changes between baseline and imaginal imagery presentation. Levin et al. (1982) found somatic changes during imagery presentation comparable to those produced by in vivo exposure of phobic patients. Results are

consistently less marked for agoraphobics, hence the importance of development of effective paradigms for agoraphobics, and PD patients. Some believe that agoraphobic and PD patients tend to have more unstable, unpredictable fear schemas which provide a lack of consistency in the interpretations of their arousal experiences (Hibbert, 1984; Cook et al.,1988). Although Watkins et al. (1990) support this idea, they point out that this "greater complexity" should not preclude effective imaginally-induced arousal if cognitive propositions are included and sufficiently elaborated to prime physiological reactivity.

Deficits in the Literature addressed by the described study

Despite the impressive body of literature addressing various aspects of PD, a thorough understanding of the precise role and impact of psychological and cognitive variables is unclear. Although the examination of psychological models of panic has been steadily increasing since the 1980's, the empirical use of these models, either alone or in combination with biological theories, is nowhere near that of the strictly biologically-based paradigms. Furthermore, the experimental induction of panic via cognitive versus biological manipulation, is even more rare.

Examination of the role of cognitive variables in panic, precipitated via an imaginal exposure paradigm is an extension of previous work. This study not only examined the psychological and physiological effects of an imaginal exposure paradigm in the initiation of panic symptoms in PD and non-PD subjects, but additionally examined within-group variations in the response to varied subject-matter content areas described in the various vignettes. Only one (two if one treatment study is considered) study was found in the literature that had even touched on this possible content-specificity focus of panic

(Watkins et al., 1990; Clum et al., 1993). As others have pointed out, due to the enhanced complexity of the precipitating stimuli associated with PAs, hence, PD, it may initially seem that persons with PD are less responsive to arousal via imaginal paradigms. However, we believe, as Watkins and colleagues state, that if this complexity is addressed via a more detailed experimental paradigm, this "limitation" will be overcome. Only by addressing such intricacies may we better understand the nature of PD. The elicitation of panic symptoms without a biological challenge is itself a powerful demonstration of the cognitive component of PD. In addition, use of imaginal exposure to induce panic, and manipulation of the specific imaginal situations with differential responding to content-variable vignettes, would provide exciting additional avenues for the study of more specific etiological factors, as well as treatments, for panic.

In view of what is currently known, four general hypotheses are put forth:

1) Panickers will show greater overall psychological/emotional change in response to audiotaped stimuli than non-Panickers;

2) Panickers will show greater overall physiological changes (as indicated by Blood Pressure, Pulse, Mean Arterial Pressure changes) than non-Panickers;

3) Panickers who indicate a situational-specific-focus area for PA's will show greater objective (physiological) and subjective (psychological) perturbations in response to the audiotape that most closely resembles their identified content area;

4) Although Panickers will exhibit more pronounced perturbations in response to all audiotapes, it is expected that both groups will show similar differential degrees of

responding to the various audiotapes, with the lowest reactivity being elicited in response to the Neutral vignette.

Method

Subject Recruitment

PD subjects were recruited via voluntary referrals from the psychology and psychiatry outpatient clinics at a large tertiary care hospital; while normal controls were solicited to participate from previously posted advertisements for research subjects. Normal healthy individuals received monetary compensation (40 dollars).

Screening and Group Assignment

Potential subjects were contacted by telephone and administered a medical and psychological screen. Subjects with a history of cardiovascular disease, respiratory disease, seizure disorder, high blood pressure, head injury, non-correctable hearing or visual impairment(which would hamper response to auditory or written measures), hepatic or renal disease, endocrinological disease (i.e., diabetes); and, currently pregnant women were excluded. A psychiatric history of bipolar disorder or seizures, or current primary DSM-IV diagnosis other than PD (including alcohol or other chemical dependency treatment; or current psychoactive substance use) precluded acceptance as a subject.

Subjects were assigned to either a PD or Normal control group based diagnostic status derived from the Structured Clinical Interview for the DSM-IV. The SCIDs were administered by one of three comparably-trained clinical psychology doctoral students. Anyone meeting criteria for a primary DSM-IV diagnosis other than PD was excluded from assignment to the PD group.

The sample was comprised of 36 subjects (19 women, 17 men) divided into two groups of PD (9 women, 11 men) and non-PD healthy controls (10 women, 6 men). They

ranged in age from 18-56 years with a mean of 31 years. See Table 1 for demographics and Table 2 for clinical characteristics.

Design

The study employed a two-factor between group (Panickers, Non-Panickers) repeated measures design, with each tape repeated twice; group status being the assigned factor, and tape order being the repeated factor administered in counter-balanced fashion. A within-subjects multivariate analysis of response differences to the 4 different specific-content-focus audiotapes was performed and compared to baseline.

General Assessment Procedure

Following the telephone screen, eligible subjects were scheduled to participate in the experiment. Subjects were seated in a comfortable chair in a well-lit room. Following informed consent, subjects completed an assessment battery which included: a demographic questionnaire and a medical and psychological history (including medication history) in order to detect and screen out any individuals who had exclusionary conditions not previously detected. After these initial procedures, subjects were asked to complete a variety of self-report measures, reading instructions thoroughly and directing any questions to the examiner. The self report measures included the Acute Panic Inventory (API), the Beck Depression Inventory (BDI), the Sheehan Patient Rating Anxiety Scale (SPRAS), the Fear Questionnaire-Agoraphobia Subscale (FQ), the Panic Appraisal Inventory (PAI), the Anxiety Sensitivity Index (ASI), the Sheehan Disability Scale (SDS), and the Mobility Inventory for Agoraphobia.

Following completion of these measures, as well as demographic and medical screening questionnaires, each subject was interviewed by a clinical psychology doctoral student using the Structured Clinical Interview for DSM-IV. All SCID interviews were videotaped, with consent, so that any ambiguity in diagnosis or questions regarding standardization of interviews could be examined as needed. All of the healthy control subjects were determined to be free of any Axis I disorder. All patients with PD as a primary diagnosis were assigned to the PD group.

Each subject was seated in a comfortable chair in a semi-reclined position, with feet elevated and back at approximately a 45-degree angle. Each subject was given the following verbal instruction:

"You will be asked to listen to several stories, one at a time, which describe a person experiencing different situations. Each story is on a tape and repeated so that you will hear the same story twice."

Following this instruction, the blood pressure cuff was attached to the left upper arm per the manufacturer's instructions, and the apparatus was set for one-minute intervals. The following verbal instruction was then dictated:

"This will measure heart rate and blood pressure during the experiment. You need to sit quietly for several minutes while we make sure the equipment is working properly."

The subject was then allowed to sit for 5 minutes, with the examiner outside the room, to establish a baseline. After 5 minutes, the examiner returned, marked the end of the baseline period on the monitoring strip, and handed the subject the baseline API, dictating:

"Please fill this out according to how you were feeling during the past 5 minutes."

While the subject was completing this measure, the examiner was outside the room, selecting audiotape order at random, and marking the tape order on the 4 experimental API forms. After the subject completed the baseline API, the examiner returned, taking the completed measure and dictating the general instruction:

"Simply sit back in the chair, close your eyes, and listen to the first story. Try to imagine yourself, as best as you can, experiencing the same things that are going on in the story. You will complete several forms after each story."

Then, as an introduction to the first vignette:

"The story will describe in detail the thoughts and feelings someone might experience in a situation. Allow yourself, as best as you can, to "get into the shoes" of the person being described. Try to imagine yourself feeling and thinking what they are experiencing.

The examiner then placed the tape recorder on the table, out of the patient's reach, started the tape, and left the room, closing the door.

Upon conclusion of the first tape, the examiner returned to the room, marked the end of the first tape on the monitoring strip, and handed the subject the first experimental API, stating:

"Please fill this out according to how you felt during the first tape."

The examiner then left the room, taking the tape recorder in order to prepare the second tape. Upon the subject's completion of the first API, the examiner returned to the room, marked the end of the first tape on the monitoring strip and dictated:

"This is another story. Remember to allow yourself, as best as you can, to "get into the shoes" of the person being described. Try to imagine yourself feeling and thinking what they are experiencing as you hear the story."

The examiner then started the second tape, leaving the room.

Upon conclusion of the second tape, the examiner returned to the room, marked the end of the second tape on the monitoring strip, handed the subject he second API, stating:

"Please fill this out according to how you felt during the tape."

The examiner then left the room, taking the tape recorder in order to prepare the third tape. Upon the subject's completion of the second API, the examiner returned, took the completed measure, and dictated:

"This is another story. Remember to allow yourself, as best as you can, to "get into the shoes" of the person being described. Try to imagine yourself feeling and thinking what they are experiencing as you hear the story."

The examiner then started the third tape, leaving the room.

Upon conclusion of the third tape, the examiner returned, marked the end of the third tape on the monitoring strip, and stated:

"Please fill this out according to how you felt during the tape."

The examiner handed the subject the third API and left the room.

Upon completion of the third API, the examiner returned, taking the completed measure, and dictated:

"This is the final story. Remember to allow yourself, as best as you can, to "get into the shoes" of the person being described. Try to imagine yourself feeling and thinking what they are experiencing as you hear the story."

The examiner then started the fourth tape, leaving the room.

Upon conclusion of the fourth tape, the examiner returned, marked the end of fourth tape on the monitoring strip, handed the subject the fourth API, and stated:

"Please fill this out according to how you felt during the tape."

The examiner then left the room.

Upon completion of the fourth API, the examiner returned, stating:

"We are done with this part of the assessment."

Vignettes

Four types of scenes were developed for the audiotapes. The Neutral (approximately 8 minute, 20 seconds) scene described a situation in which subjects felt neither entirely calm nor entirely anxious (an outdoor scene involving casual social interaction with a slow-paced non-high-stress task activity (helping a man find his fishing pole that was dropped into a pond) was described. The Physical Threat (approximately 4 minutes, 20 seconds duration) tape described a common interoceptive stimuli focus situation (escalating cardiac symptoms) for PD patients. The Social Threat (approximately 8 minutes) scene described a common social embarrassment/humiliation scenario (inept public speaking) common to some PD patients. The Loss-of-Control Threat (approximately 7 minutes duration) scene described a common setting frequently associated with loss-of-control fears in PD patients (driving an automobile on a crowded highway).

Each tape contained the given scenario, repeated so the subject would hear each story twice. Each subject was given information and instructions following the devised "Vignette Study Protocol" (see Appendix O). Before completion of a baseline API, intructions were given regarding what would occur (..several stories, one at a time, which describe a person experiencing different situations. Each story is on a tape and repeated so that you will hear the same story twice). Additional instructions were given prior to and immediately upon cessation of each audiotape. These included preparatory instruction (..The story will describe in detail the thoughts and feelings someone might experience in a situation. Allow yourself, as best as you can, to "get into the shoes" of the person being described. Try to imagine yourself, as best as you can..feeling and thinking what they are experiencing). Brief post-tape instructions were given with administration of each API (Please fill this out according to how you felt during that tape).

Psychophysiological Measures

Objective measurement of physiological responses (HR, Systolic and Diastolic BP, MAP) was simultaneously recorded using the Dinamap Vital Signs Monitor, Model 1846 SX (Critikon) system. Measurements were taken at 1 minute intervals set on the system, with the blood pressure cuff attached per manufacturer's instructions to each subject's left upper arm. A five minute period preceded the Vignette Study Protocol in order to establish familiarity with the sensations produced by the apparatus prior to establishment of a baseline. The machine was faced away from the seated subject so patient perceptions would not be affected by readings displayed by the machine's digital display or monitoring strip.

Psychological Measures(Dependent Variables)

Subjective measurement of psychological responses was measured via administration of the API at baseline and within 1 minute after completion of each scenario. Self-report measures are described below.

The modified API is a 24-item inventory of panic-related symptoms. Each item is rated on a 0 to 3 point scale (0=absence of stated symptom; 1=mild severity; 2=moderate severity; 3=severe). Prior to implementation of experimental stimuli, each subject is asked to complete a baseline API of current symptomatology (i.e., "how you felt during the past 5 minutes" (just waiting, relaxing in chair with experimenter out of room). This procedure is repeated after each audiotaped vignette, requesting the subject to "please fill this out according to how you felt during the tape). Vignettes (4 total) were presented in counterbalanced order to control for practice and order effects.

The Anxiety Sensitivity Index (ASI) measures fear associated with various physical sensations that are commonly linked with anxiety (Reiss, Peterson, Gursky and McNally, 1986). It consists of a 16-item self-report inventory in which the subject is asked to rate the extent to which he agrees with each item via selection of one of five points on a Likert scale. The scale responses range from "very little" (0) to "very much" (4). The ASI has a high level of internal consistency, with alpha coefficients ranging from .82 to .91 (Peterson & Reiss, 1992). Additionally, it has satisfactory test-retest reliability over 3 years of .71 (Maller and Reiss, 1992).

The Beck Depression Inventory (BDI) is a 21 item self-report inventory designed to measure the subjective severity of depressive symptomatology. The 21 items, which are

sets of statements, are answered on a scale ranging from 0 (denial of complaint) to 3 (endorsement of highest level of complaint) regarding severity of depressive-related feelings and behaviors. Instructions ask the respondent to report such symptoms as experience during the preceding week, "including today." The internal consistency according to Cronbach's coefficient alpha ranged from .73 to .95 over analysis of 25 studies (Beck, Steer, and Garbin, 1988). Pearson correlation coefficients for the nonpsychiatric samples ranged from .60 to .83. The test-retest reliability showed correlations ranging from .48 to .86 with psychiatric samples and .60 to .90 with nonpsychiatric samples.

The Fear Questionnaire (Agoraphobia Subscale) is used to assess agoraphobic avoidance behavior. It consists of 5/15 of the FQ items, omitting those which focus on blood or injury phobia or social phobia. The subject rates the degree of agoraphobic avoidance to the situation or object outlined in each item. The agoraphobia subscale has been found to exhibit adequate psychometric properties and is the most commonly used self-report measure for assessing agoraphobia in treatment-outcome research (Jacobsen, Wilson, and Tupper, 1988).

The PAI consists of three specific areas specifically related to panic. The first asks the individual to rate the likelihood that he would panic during each of the 15 activities listed. This rating is based upon a continuum ranging from "no chance of panic" (0) to "definite panic" (100). The second area asks the individual to rate the specific types of panic-related appraisals relative to three specific threat domains (physical, social, or loss of control). This also ranges from 0 (not at all troubling), to 100 (extremely troubling). In

the third section, three ratings are made regarding the individual's subjective ability to effectively cope with panic attacks in a variety of listed situations. This scale ranges from 0 (not at all confident) to 100 (completely confident) (Telch et al., 1988).

The SPRAS is a 35-item self-report scale for assessment of the intensity of anxiety symptoms (Sheehan, 1983). Each symptom (e.g. trembling or shaking) is rated on a five-point scale ranging from 0 (not at all distressing) to 4 (extremely distressing). The instructions were modified so that symptom ratings were based upon a one-week time period.

The Mobility Inventory (MI) is a 27-item questionnaire primarily designed to assess agoraphobic avoidance behavior. The subject is instructed to rate the severity of avoidance in situations where he is alone or accompanied. The Avoidance When Alone subscale is particularly reliable (r=.90), shows good internal consistency (alpha=.94), and has good discriminative utility with agoraphobic and nonagoraphobic individuals (r=.80) (Chambless, Caputo, Jason, Gracely, and Williams, 1985).

The Sheehan Disability Scale (SDS) is a four-item self-report measure of global impairment attributable to the presenting problem (Ballenger et al., 1988). Three of the items assess impairment in: (a) work activities; (B) social life and leisure activities; and (c) family life and home responsibilities. Each item is rated on an 11-point Likert scale (0 = not at all, 1-3 = mild, 4-6 = moderate, 7-9 = marked, 10 = severe). The remaining item assesses overall work and social disability and is scored on a five-point scale.

The Medical Screening Questionnaire used assessed personal medical history, mental health history, family medical history, and current health status.

Results

Analytic Overview

Baseline differences between groups [Panic Disorder (PD) versus Normal Controls (NC)] on demographic and clinical variables were examined using independent t-tests for continuous variables and chi-squares for nominal variables. Group (PD, NLC) and Tape [(Loss of Control Threat, Social Threat {B}, Physical Threat {C}, and Control {D}]) regression analyses were used to assess the relationship between physiological and subjective responding to each of the audiotaped vignettes.

Group Differences on Demographic and Clinical Variables

Demographic variables are presented in Table 1. There were no statistically significant group differences in age, gender, ethnicity, education, or employment (p's > .05). Marital Status was found to be statistically significant (x^2=7.37,p < .05) with PD patients more likely to be married and NC's more likely never married

Means and standard deviations on the clinical variables for PD patients and NLC patients are presented in Table 2. As expected, the two groups differed on measures of anxiety (SPRAS-1), phobic avoidance (FQ-Ago), fear of fear (ASI Total), impairment (SDS Total), panic appraisal likelihood (PAI-1), panic appraisal-core threats total (PAI-2), panic appraisal-physical threats (PAI-P), panic appraisal-social threats (PAI-S), panic appraisal-loss of control (PAI-2-L), panic appraisal-coping (PAI-3), and depressive symptoms (BDI). All of these differences were highly significant (ps < .01).

With regard to panic attack (PA) frequency , PD patients reported a mean of 3.2 full-symptom PAs and 31.2 limited-symptom PAs in the past month.

Insert Tables 1 & 2 about here

Group Differences on Subjective and Physiological Responding Measures

Examination of subjective (SUDS, symptoms) and physiological (HR, SBP, DBP, MAP) indices at baseline revealed higher baseline scores on all indices for PD versus NC subjects (See Table 3). That is, at baseline, prior to experimental manipulation, PD subjects exhibited higher SUDS and API scores as well as higher levels of physiological arousal.

Psychological Responses to Imaginal Threat Scenarios

Multiple regression analyses were used to examine changes in emotional responding to the four (3 experimental, 1 control) tapes (see Table **4?).**

Controlling for baseline levels, logistic regression was used to predict subjective anxiety (SUDS) and symptom (API) ratings. There were significant group differences ($p < .05$) in predicted SUDS in response to both the loss of control (A) and social (B) threat tapes. There were significant group differences in predicted API totals in response to all four (A-D) of the audiotaped vignettes ($p < .01$).

Insert Tables 5 & 6 about here

Reported Panic in Response to Imaginal Exposure

Examination of reported PAs to imaginal threat scenarios indicated a significant group difference with an overall total of 20% of PD patients (12 of 60 exposures) and 4% of NLC patients (2 of 48 exposures) reporting subjective panic in response to one or more of the tapes.

Insert Table 6 about here

With regard to the induction of panic, the loss of control threat (tape A) scenario was the most effective in selectively inducing panic (in 30% of PD subjects) in PD subjects but not in normals (0% of NLC's).

While social (B) and physical (C) threat scenarios were less effective than loss of control, they were equally effective in comparison with one another in inducing panic in PD subjects (15%). However, the physical threat (C) tape, much like the loss of control tape, showed no precipitation of panic in normals, while the social threat (B) scenario was almost as effective in inducing panic in normals as in panickers (13%). Furthermore, the social threat scenario was the only vignette to which any normals reported panic responses.

The control tape (D), as expected, did not induce panic in normals, but did induce panic in one PD subject.

Physiological Responses to Imaginal Threats

Controlling for baseline, multiple regression analyses were used to examine the relationship between the subjects' baseline physiological indices (heartrate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) and changes in physiological responding to the four (3 experimental, 1 control) tapes.

Insert Tables 7,8.9, & 10 about here

There were significant group differences in predicted HR in response to all four (A-D) of the tapes ($p < .01$) (see Table 8). There were significant group differences in predicted SBP in response to the loss of control (A), physical (C), and control (D), tapes ($p < .01$) (see Table 9). There were significant group differences in predicted DBP in response to all four (A-D) of the tapes ($p < .01$) (see Table 10). There were significant group differences in predicted MAP in response to all four (A-D) of the tapes ($p < .01$) (see Table 11).

Insert Table 10 about here

Specific Threat Correlations between PAI and Tape Scenarios

Pair-wise correlations between PAI subscales (physical-P, social-S, loss of control-L) and psychological and physiological responding scores during their content-congruent and content-incongruent tapes was performed.

Overall, subjective psychological measures (SUDS, API) showed the highest correlations with PAI items, particularly those with a social or loss of control focus. Physiological indices (HR, SBP, DBP, MAP) showed the lowest overall correlations with PAI scores, and the physical focus subscale of the PAI showed poor overall correlations with almost all indices with the exception of a significant positive correlation with SBP ($p < .05$) and negative correlation with MAP ($p < .05$) during the control tape.

Physiologically, the only other significant correlations were found between the social subscale of the PAI, and SBP during the loss of control (A) and control (D) tapes ($p < .01$).

With regards to psychological indices, the social and loss of control subscales of the PAI showed some statistically significant correlations with SUDS and API scores. SUDS scores during the loss of control scenario were highly correlated with loss of control subscale (PAI-L) scores ($p < .01$). SUDS scores during the loss of control scenario were equally correlated with physical subscale (PAI-P) scores ($p < .01$), but not with the social or control tapes.

SUDS scores during all three experimental (but not control) tapes were highly correlated (social $p < .05$, loss of control $p < .01$, physical $p < .01$) with social threat subscale scores on the PAI-S.

With regards to API scores, the loss of control subscale of the PAI showed the highest correlation ($p < .01$) with the loss of control threat tape (A), but was significantly correlated with the physical threat tape (C) as well ($p < .05$).

The social focus subscale of the PAI showed the highest correlation ($p < .01$) with the physical threat (C) tape, but was also significantly correlated ($p < .05$) with the loss of control threat (A) tape as well. The PAI-P and physical threat tape (C) did not show significant correlations. As stated, the PAI-P tended to show a lack of correlation with all psychological indices and most physiological indices.

Insert Table 11 about here

Discussion

The present study is one of the first to examine the efficacy of imaginal exposure in the precipitation of panic attacks (PAs). This study differed from previous investigations in several respects. First, unlike Watkins et al.'s (1990) study of imagery-induced arousal in PD patients, we included a normal control group. Second, this study utilized more comprehensive physiological assessments that included not only heart rate (HR), but systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP). Third, we included API data as well as SUDS data as subjective measures of anxiety symptoms. Finally, unlike previous studies (e.g., Cook et al., 1989; Watkins et al., 1990; Clum et al., 1993) we examined the content-related, situational-specific-focus aspects of PAs in our subjects in an attempt to explore the specificity of PAs more closely.

Based upon psychological models of panic (Beck, Emery, and Greenberg, 1985; Clark , 1986) we expected that PD patients would show greater overall psychological/emotional changes in response to audiotaped stimuli than NC subjects. Overall, this hypothesis was not well supported. Although PD patients presented with higher levels of baseline arousal, they did not demonstrate significantly higher subjective changes, compared to NCs, in response to any of the four (A-D) audiotapes. However, there were trends toward increased subjective anxiety in PD patients' responses to the Loss of Control (A) and Physical (C) threat tapes as measured by increased SUDS ratings. Although results were less impressive than anticipated, these findings are consistent with and supportive of psychological models of panic which describe PD

subjects as being more emotionally or psychologically aroused in general, as well as being more emotionally/psychologically reactive, or hyperresponsive, to stimuli (e.g., Beck and Rush, 1975; Beck, Emery, and Greenberg, 1985; Beck, 1988; Clark, 1986; Goldstein and Chambless, 1978).

An interesting exception to the expected findings occurred in response to the Social (B) threat tape. Here, although PD patients did show higher Mean SUDS and API scores than NCs, the anticipated change scores compared to baseline were reversed, with PD subjects exhibiting the lowest change from their more-aroused baseline, and NCs reporting higher changes in both Mean SUDS and API scores as compared to their unaroused baseline. So, although NCs were much less aroused at baseline, as a group, they appeared more reactive to the Social (B) threat scenario. At least two possible explanations exist. First, there could be a small number of subjects within the NC group who are subdiagnostic for social phobia, and, undetected by pre-assessment measures, their uncharacteristically "high for normal" scores may be skewing the data for the relatively small (N=16) normal sample. Second this finding may be due to the high base-rate levels of socially-specific anxiety that exist in the general population. Normals in general may be quite susceptible to socially-focused threats, with a high percentage of them having increased SUDS and API scores. Our sample showed this tendency, with no normals reporting a panic response to any scenario except social threat, and with the majority of normal subjects reporting SUDS scores at or above their high Mean SUDS.

Data providing stronger support of the evidence of PD subjects' greater psychological/emotional responding was found in the subjectively reported panic

responses. While some PD patients panicked in response to all of the audiotapes (even one in response to the neutral Control tape), NCs did not report panic to any tape except the Social (B) threat scenario. Overall, 20% of the PD patient exposures to experimental threat stimuli (tapes A-C) resulted in subjective panic. In contrast, only 4% of the NC patient exposures to experimental threat stimuli resulted in subjective panic.

W also expected that PD patients would show greater overall physiological changes (as indicated by HR, SBP, DBP, MAP) in response to audiotaped stimuli than NC subjects. This hypothesis was not supported. Although PD patients initially presented with, and continued to exhibit, higher levels of physiological arousal across all indices, they did not vary sufficiently from baseline levels to be meaningful. That is, PD subjects demonstrated greater physiological arousal (as measured by HR, SBP, DBP, and MAP) at baseline compared to NCs, and, although they maintained this higher level of arousal as compared to their NC counterparts, their physiological reactivity to the stimuli was not seem hyperreactive. At least two explanations exist. First, PD subjects may have arrived with, and maintained a high level of physiological arousal that did not remit. This high level of baseline arousal, whether it was due to a generally-aroused state, or due to anticipatory anxiety associated with the experiment, may have obfuscated any physiological reactions to the stimuli, if they were present. Although there are conflicting findings in the empirical literature, this is consistent with biological-challenge studies that have found increased resting heart rate in PD patients, interpreted by some (e.g., Liebowitz et al., 1985) as indicative that PD patients who exhibit panic in response to biological challenge (e.g., sodium lactate infusion) are physiologically "primed" to panic (

Bond, James, and Lader, 1974; Kelly, Mitchell-Heggs, and Sherman, 1971; Nesse et al., 1984). Alternatively, and in concert with more strict cognitive models of panic, these findings may provide support for the idea that it is PD subjects' cognitive misinterpretation of environmental cues that causes them to appraise stimuli as threatening. Therefore, although they may believe they are becoming increasingly physiologically aroused due to internal or external stimuli; in fact, their increased arousal has a purely cognitive-perceptual origin. Thus, increases in subjective measures of arousal without increases in physiological indices, makes sense. This is consistent with other challenge studies of PD that indicate no group differences in baseline responding despite significant group differences in subjective responding (Yeragani et al., 1986; Yeragani et al., 1987). Additional support for this finding is also found in recent anxiety literature that focuses on social phobics. Hofmann et al. (1995) found inconsistencies between physiological and subjective arousal in subjects with social phobia (public speaking). Although social phobics with avoidant personality disorder reported more subjective anxiety than either pure social phobics or normals, the social phobics with avoidant personality disorder did not exhibit the heart rate differences from normals that the pure social phobics showed. So, although they reported the highest subjective anxiety, they did not demonstrate higher physiological arousal as measured by heart rate. This lack of consistent heart rate change is also consistent with work by Lang and his colleagues (Lang, 1968; Cook et al., 1988).

In our study, it was expected that even if PD subjects did exhibit more pronounced perturbations in response to all audiotapes, both groups would show similar differential degrees of responding to the various audiotapes, with the lowest reactivity elicited in

response to the neutral Control (D) vignette. This hypothesis was supported. Both groups showed the lowest scores on subjective and physiological responding measures in response to the neutral Control (D) vignette. This supports the integrity of the experimental manipulation. As discussed, the subjective psychological measures proved to be much more sensitive than the physiological indices, although, overall, the lowest measures of physiological arousal were found during the neutral Control vignette (even lower than baseline scores) suggesting that the control tape was relaxing.

It was expected that PD patients who identified a situation-specific-focus area for their PAs would show greater physiological and subjective perturbations in response to the audiotape that most closely resembles their identified (via the PAI) content. This hypothesis was partially supported. Overall, subjective psychological measures (SUDS, API) showed the highest correlations with PAI items, particularly those with a social or loss of control focus. Correlations between subjective measures and PAI subscales were good overall, except in regards to the Physical (C) threat tape. There were differential effects of the variable-content threat stimuli, suggesting that not only is imaginal exposure effective in precipitating panic, but differential responding to specific content scenarios does exist.

Unfortunately, although there were some effects of specificity, there was some overlap as well in that the specific focus of the threat tapes did not always correlate highest with the content-congruent PAI subscale. Since there is some probable overlap of cognitions and physiological symptoms regardless of the threat focus (e.g., Loss of Control, Social), it is difficult to obtain as much discriminatory power as one would like.

Further refinement in relationship to enhancing discriminative validity of imaginal stimuli would be valuable.

In sum, although our findings were generally supportive of those in previous studies (e.g., Cook et al., 1989; Watkins et al., 1990; Clum et al., 1993) that utilized imaginal exposure, our findings were not as powerful, particularly with regard to physiological indices. Although Watkins et al. found significant HR elevations with stress and panic imagery, and not with neutral or relaxing scenarios, our subjects did not exhibit such dramatically distinct responses. Although we did incorporate the threatening "catastrophic cognition" element (some potentially fearful ideas or consequences such as "am I having a heart attack?") that they suggested to increase the likelihood of a panic response; in our attempts to provide more specificity of focus in the content of the scenarios we may not have included enough of this aspect in the social threat scenario, perhaps making it less threatening to our PD patients than the other two threat vignettes. In addition, the largely unavoidable overlap of threat areas made it difficult to delineate the specific content areas optimally. The incorporation of some aspects of physical threat into the loss of control scenario and vice-versa was particularly difficult. It may be found with further study that the loss of control threat is of particular significance to PD patients, and the presence or absence of this construct is the critical factor in imaginal induction of panic. Although this element is also found in a social threat scenario, it may not be comparable in it's potentially catastrophic implications or relevance (e.g., threat of serious injury or death).

References

American Psychiatric Association. (1994) Diagnostic and statistical manual of mental disorders (4th ed.). Washington, DC: Author.

American Psychiatric Association. (1987). Diagnostic and statistical manual of mental disorders (3rd ed., revised). Washington, DC: Author.

American Psychiatric Association. (1984). Diagnostic and statistical manual of mental disorders (3rd ed.) Washington, DC: Author.

Anderson, D.J., Noyes, R., & Crowe, R.R. (1984). A comparison of panic disorder and generalized anxiety. Journal of Psychiatry, 141, 572-575.

Antony, M.M., Brown, T.A., Craske, M.G.,Barlow, D.H., Mitchell, W.B., & Meadows, E.A. (1990). Accuracy of heart rate estimation in panic disorder, social phobic, and non-anxious subjects. Poster presented at the 24th annual AABT meeting. San Francisco, CA.

Ballenger, J.C., Burrows, G.D., DuPont, R.L., Jr., Lesser, I.M., Noyes, R., Jr., Pecknold, J.C., Rifkin, A., & Swinson, R.P. (1988). Alprazolam in panic disorder and agoraphobia: Results from a multicenter trial. Archives of General Psychiatry, 45, 413-422.

Barlow, D.H., Vermilyea, J., Blanchard, E.B., Vermiliyea, B.B., DiNardo, P.A., & Cerny, J.A. (1985). The phenomenon of panic. Journal of Abnormal Psychology, 94, 320-328.

Barlow, D.H.B. (1988). Anxiety and its disorders: The nature and treatment of anxiety and panic. New York: Guilford Press.

Beck, A.T. (1988). Cognitive approaches to panic disorder: Theory and therapy. In S. Rachman & T.J. Maser (Eds.), Panic: Psychological perspectives (pp. 91-109). Hillsdale: NJ: Erlbaum.

Beck, A.T., & Rush, A.J. (1975). A cognitive model of anxiety formation and anxiety resolution. In I.G. Sarason & C.D. Spielberger (Eds.), Stress and anxiety, Vol. 2. Sydney: Wiley & Sons.

Beck, A.T., & Emery, G.D. (1979). Cognitive Therapy of Anxiety and phobic disorders. Manual of Center for Cognitive Therapy, 133 South 36th St., Philadelphia, PA 19104.

Beck, A.T. , & Rush, A.J. (1985). A cognitive model of anxiety formation and anxiety resolution. Special Issue: Stress and anxiety. Issues in Mental Health Nursing. 7(1-4), 349-365.

Beck, A.T., Emery, G.D., & Greenberg, R.L. (1985). Anxiety Disorders and Phobics. Basic Books: New York.

Berg, I., Butler, A., & Pritchard, J. (1974). Psychiatric illnesses in the mothers of school-phobic adolescents. British Journal of Psychiatry, 125, 466-467.

Bond, A.J., James, C., & Lader, M.H. (1974). Physiological and psychological measures in anxious patients. Psychological Medicine, 4, 364-373.

Bowlby, J. (1969). Attachment and Loss; Vol. I, Attachment. Basic Books: New York.

Bowlby, J. (1973). Attachment and Loss; Vol. II, Separation, Anxiety, and Anger. Basic Books: New York.

Brehony, K.A. , & Geller, E.S. (1981). Agoraphobia: appraisal of research and a proposal for an integrative model. In Progress in Behavior Modification, Vol. 12, (Edited by Hersen, M., Eisler, R., and Miller, P.). Academic Press: New York.

Butler, K.S. , & Rapee, R.M. (1991). The influence of anxiety on accuracy of heart rate estimation. Behaviour Change, 8, 117-123.

Carey, G. , & Gottesman, I.I. (1981). Twin and family studies of anxiety, phobic. and obsessive disorders. In Anxiety: New Research and Changing Concepts (Edited by Klein D.F. and Rabkin J.). Raven Press: New York.

Carr, D.B. & Sheehan, D.V. (1984). Evidence that panic disorder has a metabolic cause. In Biology of Agoraphobia (Edited by Ballenger J.C.). American Psychiatry Press: Washington, D.C.

Carter, M.M., Hollon, S.D., Carson, R., & Shelton, R.C. (1995). Effects of a safe person on induced distress following a biological challenge in panic disorder with agoraphobia. Journal of Abnormal Psychology, 104, 156-163.

Chambless, D.L. (1982). Characteristics of agoraphobics. In Agoraphobia: Multiple perspectives on Theory and Treatment. (Edited by Chambless D.L. and Goldstein A.J.). Wiley: New York.

Chambless, D.L, Caputo, G.C., Jasin, S.E., Gracely, E.J., & Williams, C. (1985). The mobility inventory for agoraphobia. Behaviour Research and Therapy, 23, 35-44.

Chambless, D.L. , Gracely, E.J. , (1989). Fear of fear and the anxiety disorders. Cognitive Therapy and Research, 13,9-20.

Chouinard, G. , Annable, L. , Fontaine, R. , & Solyom, L. (1982). Alprazolam in the treatment of generalized anxiety and panic disorders: a double-blind placebo-controlled study. Psychopharmacology, 77, 229-233.

Clark, D. M. (1986). A cognitive approach to panic. Behaviour Research and Therapy, 24, 461-470.

Clark, D.M. , Salkovskis, P.M., Gelder, M., Koehler, C., Martin, M., Anastasiades, P., Hackmann, A., Middleton, H., & Heavons, A. (1988). Tests of a cognitive theory of panic. In I. Hand & H.U. Wittchen (Eds.), Panic and phobias 2. Berlin: Springer-Verlag.

Clum, G.A., Watkins, P.L., Borden, J.W., Broyles, S.E., & Hayes, J. (1993). A comparison of guided imaginal coping and imaginal exposure in the treatment of panic disorder. Journal of Rational-Emotive & Cognitive-Behavior Therapy, 11(4), 179-193.

Cohen, M.E. , & White, P.D. (1950). Life situations, emotions and neurocirculatory asthenia (anxiety neurosis, neurasthenia, effort syndrome) Association for Research in Nervous and Mental Disease Proceedings, 29, 832-869.

Cook, E.W. III , Melamed, B.G. , Cuthbert,B.N. , McNeil, D.W. , & Lang, P.J. (1988). Emotional imagery and the differential diagnosis of anxiety. Journal of Consulting and Clinical Psychology, 56, 734-740.

den Boer, J.A. , Westenberg, H.G., Klompmakers, A.A. , & Van Lint, L.E. (1989). Behavioral biochemical and neuroendocrine concomitants of lactate-induced panic anxiety. Biological Psychiatry, 26(6), 612-622.

Ehlers, A. , Margraf, J., Roth, W.T., Taylor, C.B., Madduck, R.J., Sheikh, J., Kopell, M.L., McClenahan, K.L., Gossard, D., Blowers, G., Agras, W.S., & Kopell, B.S. (1986). Lactate infusions and panic attacks: Do patients and controls respond differently? Psychiatric Research , 17, 295-308.

Ehlers, A., & Breuer, P. (1992). Increased cardiac awareness in panic disorder. Journal of Abnormal Psychology, 101(3), 371-382.

Ehlers, A., & Breuer, P. (1995). Selective attention to physical threat in subjects with panic attacks and specific phobias. Journal of Anxiety Disorders, 9(1), 11-31.

Ehlers, A. , Margraf, J., Roth, W.T. , Taylor, C.B. , & Birbaumer, N. (1988). Anxiety induced by false heart rate feedback in patients with panic disorder. Behaviour Research and Therapy, 26(1), 1-12.

Finlay-Jones, R. , & Brown, G.W. (1981). Types of stressful life event and the onset of anxiety and depressive disorders. Psychological Medicine, 11, 801-815.

Freedman, D.X. & Glass, R.M. (1984). Psychiatry. Journal of American Medical Association, 252, 2223-2228.

Frankl,V.E. (1975). Paradoxical intention and dereflection. Psychotherapy, 12, 226-237.

Gittelman-Klein, R. , Klein, D.F. (1984). Relationship between separation anxiety and panic and agoraphobia. Psychopathology, (Suppl.), 17, 56-65.

Goldstein, A.J. , & Chambless, D.L. (1978). A reanalysis of agoraphobia. Behavior Therapy, 9, 47-59.

Griez, E., & van den Hout, M.A. (1983). Treatment of phobophobia by exposure to CO2-induced anxiety. Journal of Nervous and Mental Disease, 171, 506-508.

Hibbert, G.A. (1984). Ideational components of anxiety: Their origin and content. British Journal of Psychiatry, 144, 618-624.

Hofmann, S.G., Ehlers, A., Newman, M.G., & Roth, W.T. (1995). Psychophysiological differences between subgroups of social phobia. Journal of Abnormal Psychology, 104(1), 224-231.

Kelly, D., Mitchell-Hegss, N., & Sherman, D. (1971). Anxiety and the effects of sodium lactate assessed clinically and physiologically. British Journal of Psychiatry, 119, 129-141.

Kenardy, J., Evans, L., & Oei, T.P.S (1988). The importance of cognitions in panic attacks. Behavior Therapy. 19, 471-483.

Klein, D.F. (1964). Delineation of two drug-responsive anxiety syndromes. Psychopharmacologia, 5, 397-408.

Klein, D.F. (1980). Anxiety reconceptualized. Comprehensive Psychiatry, 21, 411-427.

Klein, D.F. (1981). Anxiety reconceptualized. In D.F. Klein & J.G. Rabkin (Eds.), Anxiety: New research and changing concepts (pp. 235-263). New York: Raven Press.

Klein, D.F. , & Fink, M. (1964). Psychiatric reaction patterns to Imipramine. American Journal of Psychiatry, 119, 432-435.

Klein, D.F. , Zitrin, C.M. , Woerner, M.G., & Ross, D.C. (1983). Treatment of phobias II. Behavior therapy and supportive psychotherapy: are there any specific ingredients? Archives of General Psychiatry, 40, 139-145.

Lader, M. (1982). Biological differentiation of anxiety, arousal, and stress. In The Biology of Anxiety. (Edited by Mathew R.J.). Brunner/Mazel, New York.

Lang, P.J. (1979). A bio-informational theory of emotional imagery. Psychophysiology, 16, 495-512.

Lang, P.J. , Levin, D.N., Miller, G.A., & Kozak, M. (1983). Fear behavior, fear imagery, and the psychcophysiology of emotion: The problem of affective response integration. Journal of Abnormal Psychiatry, 92, 276-306.

Levin, D.N, , Cook, E.W. III , & Lang, P.J. (1982). Fear imagery and fear behavior: Psychophysiological analysis of clients receiving treatment for anxiety disorders. Psychophysiology, 19, 571-572 (Abstract).

Ley, R. (1985). Agoraphobia, the panic attack and the hyperventilation syndrome. Behaviour Research and Therapy, 23, 79-81.

Liebowitz, M.R., Fyer, A.J., Gorman, J.M., Dillon, D., Davies, S., Stein, J.M., Cohen, B.S., & Klein, D.F. (1985). Specificity of lactate infusion in social phobia versus panic disorders. American Journal of Psychiatry, 142, 947-950.

MacLeod, C. , Mathews, A.M. , & Tata, P. (1986). Attentional bias in emotional disorders. Journal of Abnormal Psychology, 95(1), 15-20.

Margraf, J. , Ehlers, A. , & Roth, W.T. (1986a). Sodium lactate infusions and panic attacks: A review and critique. Psychosomatic Medicine, 48, 23-51.

Margraf, J., Ehlers, A., & Roth, W.T. (1986b). Biological models of panic disorder and agoraphobia: A review. Behaviour Research and Therapy, 24, 553-567.

Margraf, J., Taylor, C.B., Ehlers, A., Roth, W.T., & Agras, W.S. (1987). Panic attacks in the natural environment. Special Issue: Mental disorders in their natural settings: The application of time allocation and experience-sampling techniques in psychiatry. Journal of Nervous and Mental Disease, 175(9), 558-565.

Margraf, J., Ehlers, A., & Roth, W.T. (1987). Panic attack associated with perceived heart rate acceleration: A case study. Behavior Therapy, 18(1), 84-89.

Margraf, J., Ehlers, A., & Roth, W.T. (1989). Expectancy effects and hyperventilation as laboratory stressors. In H. Weiner, I. Florin, R. Murrison, & D. Hellhammer (Eds.), Frontiers of Stress Research. Toronto: Huber.

Mathews, A.M., Gelder, M.G., Johnston, D.W. (1981). Agoraphobia: Nature and Treatment: Guilford Press: New York.

Mathews, A.M., & MacLeod, C. (1985). Selective processing of threat cues in anxiety states. Behaviour Research and Therapy, 23, 563-569.

Mathews, W. , & MacLeod, C. (1986). Discrimination of threat cues without awareness in anxiety states. Journal of Abnormal Psychology, 95(2), 131-138.

McNally, R. J., & Foa, E.B. (1987). Cognition and agoraphobia: Bias in the interpretation of threat. Cognitive Therapy and Research, 11, 567-581.

McNeil, D.W. , Melamed, B.G. , Cuthbert, B.N. , & Lang, P.J. (1983). Emotional imagery and psychophysiological responsivity in simple phobia and agoraphobia. Psychophysiology, 20, 459 (Abstract).

Mefford, R. (1979). How much anxiety is "normal"? In Phenomenology and Treatment of Anxiety (Edited by Fann W.E., Karacan, I., Pokorny A.D. and Williams R.L.). Spectrum: New York.

Mendel , J.G.C. , & Klein, D.F. (1969). Anxiety attacks with subsequent agoraphobia. Comprehensive Psychiatry, 10, 190-195.

Nesse, R.M., Cameron, O.G., Curtis, G.C. , McCann, D.S., & Huber-Smith, M.J. (1984). Adrenergic function in patients with panic anxiety. Archives of General Psychiatry, 41, 771-776.

Noyes, R., Anderson, D., Clancy, J., Crowe, R., Slymen, D., Ghoneim, M., & Hinrichs, J. (1984). Diazepam and proopanolol in panic disorder and agoraphobia. Archives of General Psychiatry, 41, 287-292.

Rapee, R. (1985). Distinctions between panic disorder and generalised anxiety disorder: Clinical presentation. Australian and New Zealand Journal of Psychiatry, 19, 227-232.

Rapee, R. (1987). The psychological treatment of panic attacks: Theroretical conceptualization and review of evidence. Clinical Psychology Review, 7, 427-438.

Rapee, R.M. (1990). Psychological mechanisms underlying the response to biological challenge procedures in panic disorder. In N. McNaughton & G. Andrews (Eds.), Anxiety (pp. 75-81). Dunedin, N.Z.: Otago University Press.

Rapee, R. (1991). The contextual overlap between cognition and conditioning in clinical psychology. Special Issue: Applied learning theory: Research issues for the 1990s. Clinical Psychology Review, 11(2), 193-203.

Rapee, R., Mattick, R., & Murrell, E. (1986). Cognitive mediation in the affective component of spontaneous panic attacks. Journal of Behavior Therapy and Experimental Psychiatry, 17, 245-253.

Rapee, R.M., Sanderson, W.C. , McCauley, P.A. & DiNardo, P.A. (1992). Differences in reported symptom progile between panic disorder and other DSM-III-R anxiety disorders. Behaviour Research and Therapy, 30(1), 45-52.

Rapee, R., Telfer, L.A., & Barlow, D.H. (1991). The role of safety cues in mediating the response to inhalations of CO2 in agoraphobics. Behaviour Research and Therapy, 29, 353-355.

Rapee, R.M., Brown, T.A., Antony, M.M., & Barlow, D.H. (1992). Response to hyperentilation and inhalation of 5.5% carbon dioxide-enriched air across the DSM-III-R anxiety disorders. Journal of Abnormal Psychology, 101(3), 538-552.

Raskin, M., Peeke, H.V.S., Dickman, W. , & Pinsker, H. (1982). Panic and generalized anxiety disorders. Archives of General Psychiatry, 39, 687-689.

Reiss, S., Peterson, R.A., Gursky, D.M., & McNally, R.J. (1986). Anxiety sensitivity, anxiety frequency and the prediction of fearfulness. Behaviour Research and Therapy, 24, 1-8.

Salkovskis, P.M. , Clark, D.M. (1989). Affective responses to hyperventilation: A test of the cognitive model of panic. Behavioural Research and Therapy, 28, 51-62.

Salkovskis, P.M., & Clark, D.M. (1990). Affective responses to hyperventilation: A test of the cognitive model of panic. Behaviour Research and Therapy, 28, 51-61.

Sanderson, W.C. , Rapee, R.M., & Barlow, D.H.B. (1989). The influence of an illusion of control on panic attacks induced via inhalation of 5.5% carbon dioxide-enriched air. Archives of General Psychiatry, 46(2), 157-162.

Schachter, S., & Singer, J.E. (1962). Cognitive, social, and physiological determinants of emotional state. Psychological Review, 69, 379-399.

Shader R. , Goodman, M. , & Gever, J. (1982). Panic disorders: current perspectives. Journal of Clinical Pharmacology (Suppl.) 2, 2-10.

Sheehan, D.V. (1982a). Current perspectives in the treatment of panic and phobic disorders. Drug Therapy, 12(2), 179-193.

Sheehan, D.V. (1982b). Panic attacks and phobias. New England Journal of Medicine, 307(3), 156-158.

Sheehan, D.V. (1984).Delineation of anxiety and phobic disorders responsive to monoamine oxidase inhibitors: Implications for classification. Journal of Clinical Psychiatry, 45, 29-36.

Strategies for diagnosis and treatment of anxiety disorders. In Diagnosis and Treatment of Anxiety Disorders (Edited by Pasnau R.O.). American Psychiatric Press: Washington D.C.

Sheehan, D.V., & Sheehan, K.H. (1982a). The classification of anxiety and hysterical states. Part I. Historical review and empirical delineation. Journal of Clinical Pharmacology, 2, 235-244.

Sheehan, D.V., & Sheehan, K.H. (1982b). The classification of anxiety and hysterical states. Part II. Toward a more heuristic classification. Journal of Clinical Pharmacology, 2, 386-393.

Sheehan, D.V., & Sheehan, K.H. (1983). The classification of phobic disorders. International Journal of Psychiatric Medicine, 12, 243-266.

Soley, M.H., & Shock, N.W. (1938). The etiology of effort syndrome. The American Journal of the Medical Sciences, 196, 840-851.

Solyom, L. , Beck, P. , Solyom, C. , & Hugel, H. (1974). Some etiological factors in phobic neurosis. Canadian Psychiatric Association Journal, 19(1), 69-78.

Tearnan, B.H. , Telch, M.J. , Keefe, P. (1984). Etiology and onset of agoraphobia: a critical review. Comprehensive Psychiatry, 25(1), 51-62.

Telch, M.J., & Harrington, P.J. (1993). Anxiety sensitivity and expectedness of arousal in mediating affective response to 35% carbon dioxide inhalation. In submission.

Telch, M.J., Agras, W.S., Taylor, C.B., Roth, W.T., & Gallen, C.C. (1985). Combined pharmacological and behavioral treatment for agoraphobia. Behaviour Research and Therapy, 23(3), 325-335.

Torgersen, S. (1983). Genetic factors in anxiety disorders. Archives of General Psychiatry, 40, 1085-1089.

van den Hout, M.A. (1988). The explanation of experimental panic. In S. Rachman & J.D. Maser (Eds.), Panic: Psychological perspectives (pp. 237-257). Hillsdale, NJ: Erlbaum.

van den Hout, M.A. , & Griez, E. (1982). Cognitive factors in carbon dioxide therapy. Journal of Psychosomatic Research, 26, 209-214.

van der Molen, G.M., van den Hout, M.A. , Vroemen, J. , Lousberg, H. , & Griez, E. (1986). Cognitive determinants of lactate-induced anxiety. Behaviour Research and Therapy, 24, 677-680.

Watkins, P.L., Clum, G.A., Borden, J.W., Broyles, S., & Hayes, J. (1990). Imagery-induced arousal in individuals with panic disorder. Cognitive Therapy and Research, 14(1), 37-46.

Westphal, C. (1871). Die Agoraphobie, eine neuropathische Erscheinung. Arch. Psychiatr. Nervkrankh, 3, 138-161.

Yeragani, V.K., Balon, R., Pohl, R., Ortiz, A., Weinberg, P., & Rainey, J.M. (1987a). Do higher preinfusion heart rates predict laboratory-induced panic attacks? Biological Psychiatry, 22, 554-558.

Yeragani, V.K., Pohl, R., Rainey, J.M., Balon, R., Ortiz, A., Lycaki, H., & Gershon, S. (1987b). Pre-infusion heart rates and laboratory-induced panic anxiety. Acta Psychiatrica Scandinavica, 75, 51-54.

Zarate, R., Rapee, R.M. & Barlow, D.H. (1989). The assessment of sensitivity to panic-evoking somatic cues. Presented at the 23rd annual AABT convention. Washington, D.C., (Abstract).

Table 1

Comparison of Panic Disorder Subjects and Normal Control Subjects on Demographic Variables

Variable	PD (N=20)	NC (N=16)	Chi-Square/F Ratio
Age (yrs)			
Mean	33.1	29.0	2.71
SD	7.9	6.7	
Gender (%)			
Male	55.0	62.5	1.10
Female	45.0	37.5	
Ethnicity (%)			
Caucasian	80.0	81.3	2.97
African-American	5.0	13.0	
Hispanic	5.0	6.3	
Other	10.0	0.0	
Marital Status			
Married	70.0	31.3	7.37*
Never Married	30.0	56.3	
Divorced	0.0	12.5	
Education (%)			
High School or less	15.0	18.8	2.14
Part college(≤ 2yrs)	30.0	50.0	
College grad(≥ 4yrs)	55.0	31.2	
Employment Status (%)			
Employed	75.0	68.7	1.76
Student	15.0	12.5	
Homemaker	10.0	12.5	
Unemployed	0.0	6.3	

*p< .05 **p< .01

Table 2

Comparison of Panic Disorder Subjects and Normal Controls on Clinical Variables

Variable	PD (N=20)	NC (N=16)	F Ratio
Panic Attack Frequency(past month)			
Mean(Full-symptom)	3.2		
SD	3.9		
Mean(Limited-symptom)	31.2		
SD	65.9		
Anxiety (SPRAS-1)			
Mean	47.2	6.3	36.76**
SD	25.9	7.4	
Phobic Avoidance (FQ)			
Mean	8.6	2.7	7.32**
SD	7.3	5.2	
Fear of Fear (ASI Total)			
Mean	27.9	11.0	28.64**
SD	10.0	8.2	
Impairment (SDS Total)			
Mean	3.7	1.9	20.39**
SD	1.0	1.4	
PAI-1 (Panic Appraisal-likelihood)			
Mean	423.0	125.9	18.03**
SD	243.0	146.6	
PAI-2 (Panic Appraisal-core threats total)			
Mean	433.3	63.8	23.29**
SD	287.9	109.6	

*p< .05 **p< .01

PAI-2-P (Panic Appraisal-physical threats)			
Mean	157.2	7.5	26.69**
SD	114.8	16.5	
PAI-2-S (Panic Appraisal-social threats)			
Mean	157.8	35.0	9.35**
SD	150.2	59.8	
PAI-2-L (Panic Appraisal-loss of control)			
Mean	118.3	21.3	9.57**
SD	116.9	48.0	
PAI-3 (Panic Appraisal-coping)			
Mean	549.1	1189.1	34.62**
SD	300.7	324.1	
Depressive Symptoms (BDI)			
Mean	15.1	4.1	16.83**
SD	8.7	6.5	

*p< .05 **p< .01

Table 3

Means and Standard Deviations on Subjective and Physiological Responding Measures

		BASE		A		B		C		D	
SUDS		P	N	P	N	P	N	P	N	P	N
	M	**23**	**4**	**38**	**11**	**27**	**18**	**35**	**10**	**10**	**3**
	SD	20	13	28	18	30	27	30	16	15	8
S X S (API)											
	M	**11**	**1**	**16**	**3**	**13**	**5**	**15**	**3**	**6**	**1**
	SD	11	1	17	4	14	11	15	5	8	2
HR											
	M	**80**	**59**	**76**	**58**	**74**	**58**	**75**	**57**	**74**	**57**
	SD	15	8	15	7	14	7	14	5	13	6
SBP											
	M	**119**	**108**	**117**	**105**	**109**	**103**	**114**	**102**	**114**	**102**
	SD	15	10	10	13	26	9	13	8	13	7
DBP											
	M	**69**	**63**	**65**	**61**	**65**	**60**	**65**	**60**	**64**	**60**
	SD	9	5	9	5	8	5	9	6	10	6
MAP											
	M	**88**	**80**	**86**	**78**	**84**	**78**	**84**	**77**	**83**	**77**
	SD	11	6	10	6	9	6	10	6	10	6

Note. BASE=Measurement at baseline; A=Measurement during Tape A; B=Measurement during Tape B; C=Measurement during Tape C; D=Measurement during Tape D (control); SUDS=Subjective Units of Disress Scale (range 0-100); S X S=Signs and Symptoms; API=Acute Panic Inventory; HR=Heart Rate (beats per minute); SBP=Systolic Blood Pressure; DBP=Diastolic Blood Pressure; MAP=Mean Arterial Pressure.

Table 4 Diagnostic Status Predicting Subjective Anxiety

Covariate	Predictor	Predicted Changes in Beta value	t-ratio
Group	SUDS.Tape A	-16.42	-1.85
SUDS.base		1.08	2.34
Group	SUDS.Tape B	1.92	.18
SUDS.base		1.12	1.99
Group	SUDS.Tape C	-16.58	-1.78
SUDS.base		.82	1.70
Group	SUDS.Tape D	-4.18	-.87
SUDS.base		.32	1.25

Table 5 Diagnostic Status Predicting Subjective Symptoms

Covariate	Predictor	Predicted Changes in Beta value	t-ratio
Group	API.Tape A	-3.74	-.83
API.base		1.86	4.04
Group	API.Tape B	1.54	.36
API.base		1.76	4.05
Group	API.Tape C	-2.60	-.75
API.base		1.78	4.98
Group	API.Tape D	-1.58	-.75
API.base		.66	2.76

Table 6

Reported Panic Response numbers by Tape and Group

	PD % Panicking	NL % Panicking
A (L)	30 (6/20)	0 (0/16)
B (S)	15 (3/20)	13 (2/16)
C (P)	15 (3/20)	0 (0/16)
D (C)	5 (1/20)	0 (0/16)
Total Panic Responses to experimental tapes (A-C):	20% (12/60)	4% (2/48)

Note. (L)=Loss of Control threat scenario; (S)=Social threat scenario; (P)=Physical threat scenario; (D)=Control tape.

Table 7

Diagnostic Status Predicting Heart Rate.

Covariate	Predictor	Predicted Changes in Beta value	t-ratio
Group	HR.Tape A	.60	.37
HR.base		1.86	18.00
Group	HR.Tape B	1.44	.72
HR.base		1.68	13.16
Group	HR.Tape C	-.48	-.19
HR.base		1.60	10.18
Group	HR.Tape D	-.50	-.23
HR.base		1.58	11.87

Table 8

Diagnostic Status Predicting Systolic Blood Pressure.

Covariate	Predictor	Predicted Changes in Beta value	t-ratio
Group	SBP.Tape A	-3.16	-1.75
SBP.base		1.72	12.87
Group	SBP.Tape B	0.00	0.00
SBP.base		1.00	1.93
Group	SBP.Tape C	-.92	-.45
SBP.base		1.64	10.84
Group	SBP.Tape D	-1.36	-.80
SBP.base		1.60	12.70

Table 9

Diagnostic Status Predicting Diastolic Blood Pressure.

	Covariate	Predictor	Predicted Changes in Beta value	t-ratio
Group		DBP.Tape A	-.20	-.14
	DBP.base		1.74	8.83
Group		DBP.Tape B	-.02	-.02
	DBP.base		1.62	9.53
Group		DBP.Tape C	0.02	.01
	DBP.base		1.56	6.65
Group		DBP.Tape D	.96	.45
	DBP.base		1.70	6.11

Table 10 Diagnostic Status Predicting Mean Arterial Pressure.

Covariate	Predictor	Predicted Changes in Beta value	t-ratio
Group	MAP.Tape A	-.68	-.51
MAP.base		1.68	12.14
Group	MAP.Tape B	-.18	-.13
MAP.base		1.58	11.31
Group	MAP.Tape C	.84	.45
MAP.base		1.64	8.71
Group	MAP.Tape D	1.64	.92
MAP.base		1.62	8.88

Table 11

Specific Focus Correlations (PAI-2)

		PAI-P	PAI-S	PAI-L	PAI-Total
SUDS					
	C(P)	**.25**	.57[b]	.60[b]	.57[b]
	B(S)	.00	**.40**[a]	.27	.28
	A(L)	.25	.52[b]	**.59**[b]	.55[b]
	D(C)	.12	.09	-.01	.09
SXS(API)					
	C(P)	**.20**	.43[b]	.38[a]	.41[a]
	B(S)	.01	**.24**	.12	.15
	A(L)	.15	.36[a]	**.45**[b]	.38[a]
	D(C)	.10	-.06	-.04	.00
HR					
	C(P)	**-.15**	.20	.00	.03
	B(S)	-.25	**-.02**	-.29	-.21
	A(L)	-.27	.08	**-.03**	-.08
	D(C)	-.15	-.09	-.20	-.17
SBP					
	C(P)	**-.10**	.20	-.04	.04
	B(S)	.06	**-.18**	-.30	-.17
	A(L)	.20	.50[b]	**.27**	.40[a]
	D(C)	.40[a]	.52[b]	22	.27
DBP					
	C(P)	**-.17**	-.13	-.19	-.19
	B(S)	.18	**.09**	-.05	-.04
	A(L)	-.09	-.07	**-.07**	-.09
	D(C)	-.10	-.24	-.26	-.24
MAP					
	C(P)	**-.33**	-.19	-.40[a]	-.36[a]
	B(S)	-.25	**.12**	-.16	-.10
	A(L)	-.11	.09	**-.14**	-.05
	D(C)	-.42[a]	.06	-.12	-.18

Note. SUDS=Subjective Units of Distress Scale; SXS= Symptoms; API=Acute Panic Inventory; HR=Heart Rate in beats per minute; SBP=Systolic Blood Pressure; DBP=Diastolic Blood Pressure; MAP=Mean Arterial Pressure; (P)=Physical Sensation Threat experimental tape; (S)=Social Threat experimental tape; (L)=Loss of Control Threat experimental tape; (C)= Control tape.

[a] $p < .05$ [b] $p < .01$

APPENDICES

Analyses

1. Power and Sample Size Analyses Appendix A

Assessment Battery (in alphabetical order) **

1. Acute Panic Inventory (API) Appendix B
2. Anxiety Sensitivity Index (ASI) Appendix C
3. Beck Depression Inventory (BDI) Appendix D
4. Fear Questionnaire-Agoraphobic Subscale (FQ-Ago) Appendix E
5. Medical Screening Questionnaire Appendix F
6. Mobility Inventory for Agoraphobia (MI) Appendix G
7. Panic Appraisal Inventory (PAI) Appendix H
8. Panic Frequency Interview Appendix I
9. Sheehan Patient Rating Anxiety Scale (SPRAS) Appendix J
10. Structured Clinical Interview for Axis I DSM-IV Disorders Appendix K
11. Sheehan Disability Scale (SDS) Appendix L

Experimental Forms

1. Consent Form Appendix M
2. Demographic Information Survey Appendix N
3. Vignette Study Protocol Appendix O
4. Subject Phone Screen Interview Appendix P

**The Assesment Battery Section is not included since it contains copyrighted materials that are not available for use over the internet. Consult the thesis for this information.

Sample Size Analyses

Effect Sizes and Projected Sample Size Requirements for Some Dependent Measures
Analyses are base upon an alpha of .05 and Power of .70

MEASURE	EFFECT SIZE (d)	REQUIRED SAMPLE SIZE
Acute Panic Inventory (1)	1.70	11
Fear Questionnaire-Agoraphobic Subscale (2)	1.90	36
State Trait Anxiety Inventory (2)	5.41	36
Heart Rate (3)	1.55	12
Systolic Blood Pressure (3)	3.30	12
Diastolic Blood Pressure (3)	2.00	12
Overall Average	2.64	20

1. Beitman, Logue, Thomas & Bartels (1992).
2. Carter, Hollon, Carson, & Shelton (1995).
3. Obtained from a table found in Bystritsky & Shapiro (1992) p. 770.

Appendix B

API 1

Instructions: Please rate the severity of the symptoms your experiencing now. (For each symptom circle one number).

	Absent	Mild	Moderate	Severe
1. Do you feel faint?	0	1	2	3
2. Are you afraid of dying?	0	1	2	3
3. Are you afraid in general?	0	1	2	3
4. Do you have palpitations?	0	1	2	3
5. Is it hard for you to breathe or catch your breath?	0	1	2	3
6. Do you have an urge to urinate?	0	1	2	3
7. Do you have an urge to defecate?	0	1	2	3
8. Do you feel dizzy or lightheaded?	0	1	2	3
9. Do you feel confused at all?	0	1	2	3
10. Do things and people seem unreal?	0	1	2	3
11. Do you feel detached from part or all of your body?	0	1	2	3
12. Is it hard for you to concentrate?	0	1	2	3
13. Are you sweating at all?	0	1	2	3
14. Is it difficult for you to speak?	0	1	2	3
15. Would it be difficult for you to do your job (apart from being hooked up)?	0	1	2	3
16. Do you have any inner shakiness, twitching or trembling?	0	1	2	3
17. Do you feel nauseous or queasy?	0	1	2	3

	Absent	Mild	Moderate	Severe
18. Are you afraid of going crazy?	0	1	2	3
19. Are you afraid of losing control?	0	1	2	3
20. Do you have any tingling or numbness?	0	1	2	3
21. Are you experiencing any chest pain or discomfort?	0	1	2	3
22. Are you feeling any choking sensations?	0	1	2	3
23. Are you feeling any chills or hot flashes?	0	1	2	3
24. Are you sweating?	0	1	2	3

25. What was the **HIGHEST** level of fear anxiety you experienced during the past 9 minutes?

0 10 20 30 40 50 60 70 80 90 100

No Fear *Mild Fear* *Moderate Fear* *Severe Fear* *Extreme Fear*

API 2

Instructions: Please rate the severity of the symptoms you experienced during the last four training trials. (For each symptom circle one number).

	Absent	**Mild**	**Moderate**	**Severe**
1. Do you feel faint?	0	1	2	3
2. Are you afraid of dying?	0	1	2	3
3. Are you afraid in general?	0	1	2	3
4. Do you have palpitations?	0	1	2	3
5. Is it hard for you to breathe or catch your breath?	0	1	2	3
6. Do you have an urge to urinate?	0	1	2	3
7. Do you have an urge to defecate?	0	1	2	3
8. Do you feel dizzy or lightheaded?	0	1	2	3
9. Do you feel confused at all?	0	1	2	3
10. Do things and people seem unreal?	0	1	2	3
11. Do you feel detached from part or all of your body?	0	1	2	3
12. Is it hard for you to concentrate?	0	1	2	3
13. Are you sweating at all?	0	1	2	3
14. Is it difficult for you to speak?	0	1	2	3
15. Would it be difficult for you to do your job (apart from being hooked up)?	0	1	2	3
16. Do you have any inner shakiness, twitching or trembling?	0	1	2	3
17. Do you feel nauseous or queasy?	0	1	2	3

	Absent	Mild	Moderate	Severe
18. Are you afraid of going crazy?	0	1	2	3
19. Are you afraid of losing control?	0	1	2	3
20. Do you have any tingling or numbness?	0	1	2	3
21. Are you experiencing any chest pain or discomfort?	0	1	2	3
22. Are you feeling any choking sensations?	0	1	2	3
23. Are you feeling any chills or hot flashes?	0	1	2	3
24. Are you sweating?	0	1	2	3

25. What was the **HIGHEST** level of fear you experienced during or after the training trials?

0 10 20 30 40 50 60 70 80 90 100

No Fear *Mild Fear* *Moderate Fear* *Severe Fear* *Extreme Fear*

API 3

Instructions: Please rate the severity of the symptoms your experienced during and after the CO2 inhalation (For each symptom circle one number).

	Absent	Mild	Moderate	Severe
1. Do you feel faint?	0	1	2	3
2. Are you afraid of dying?	0	1	2	3
3. Are you afraid in general?	0	1	2	3
4. Do you have palpitations?	0	1	2	3
5. Is it hard for you to breathe or catch your breath?	0	1	2	3
6. Do you have an urge to urinate?	0	1	2	3
7. Do you have an urge to defecate?	0	1	2	3
8. Do you feel dizzy or lightheaded?	0	1	2	3
9. Do you feel confused at all?	0	1	2	3
10. Do things and people seem unreal?	0	1	2	3
11. Do you feel detached from part or all of your body?	0	1	2	3
12. Is it hard for you to concentrate?	0	1	2	3
13. Are you sweating at all?	0	1	2	3
14. Is it difficult for you to speak?	0	1	2	3
15. Would it be difficult for you to do your job (apart from being hooked up)?	0	1	2	3
16. Do you have any inner shakiness, twitching or trembling?	0	1	2	3
17. Do you feel nauseous or queasy?	0	1	2	3

	Absent	Mild	Moderate	Severe
18. Are you afraid of going crazy?	0	1	2	3
19. Are you afraid of losing control?	0	1	2	3
20. Do you have any tingling or numbness?	0	1	2	3
21. Are you experiencing any chest pain or discomfort?	0	1	2	3
22. Are you feeling any choking sensations?	0	1	2	3
23. Are you feeling any chills or hot flashes?	0	1	2	3
24. Are you sweating?	0	1	2	3

25. What was the **HIGHEST** level of fear you experienced during or after hyperventilation?

0 10 20 30 40 50 60 70 80 90 100

No Fear *Mild Fear* *Moderate Fear* *Severe Fear* *Extreme Fear*

26. Did you panic (i.e., have a sudden surge of intense anxiety) at any time during or after the CO2 inhalation? (Circle one) *1. Yes* *2. No*

USUHS Research Consent Form

Study Title: Investigation of differences in cognitive and emotional responding between patients with panic disorder and normal controls.

Principal Investigator: Dr. N. Bradley Schmidt, Ph.D.

1. Purpose of the study:

You are invited to participate in a study that is examining the differences between panic disorder patient and normal controls in emotional and cognitive responding. There will be 90 subjects in this study that will take place at the Uniformed Services University of the Health Sciences.

2. Procedures Involved in the Study:

First there will be a structured interview asking about your past and current emotional and medical history. At various times during the study you will be asked to complete questionnaires designed to measure your response before, during and after the experimental manipulation. In addition to filling out the questionnaires, you will be asked to complete a physiological assessment that will involve having your heart rate and blood pressure prior to and after inhalation of a gas that consists of a higher concentration of oxygen and carbon dioxide than you usually breathe. This mixture is not harmful or dangerous in any way. The total time to complete each assessment including the questionnaires and the physiological measures will be approximately four hours.

3. Possible Discomfort and Risks Involved:

Please note that videotaping of some parts of the assessment and treatment procedures will be conducted for reliability purposes. These videotapes will be securely stored in a locked room and viewed only by Dr. Schmidt and authorized project personnel under Dr. Schmidt's supervision. All tapes will be erased after the study is completed.

Risks to participants are extremely minimal. There are no foreseeable risks associated with the self-report assessment procedures. There are no foreseeable risks associated with the assessment of heart rate or blood pressure.

The behavioral assessment procedures are safe and have been used for many years in a variety of clinical settings. There are no foreseeable risks associated with the inhalation of oxygen and carbon dioxide gas. You have the right to refuse or discontinue participation during this or any other portion of the assessment process. In addition, Dr. Schmidt will be available in the event of crisis.

If at any time you believe you have suffered an injury or illness as a result of participating in this research project, you should contact the Office of Research Administration at the Uniformed Services University of the Health Sciences, Bethesda, MD 20814 at (301) 295-3303. This office can review the matter with you, can provide information about your rights as a subject, and may be able to identify resources available to you. Information about judicial avenues of compensation is available from the University's General Counsel at (301) 295-3028.

4. Benefits Involved:

You will receive an extensive evaluation of your emotional history. In addition, you will be compensated with a 40 dollar check. Your participation will help us in our efforts to design more effective treatments for people who suffer from panic disorder and agoraphobia.

5. Use of Research Results:

Information from your participation may appear in medical or psychological journals. Your individual identity will not be connected to any published reports.

6. Special Circumstances:

Your decision whether or not to participate will not prejudice future relations with the Uniformed Services University of the Health Sciences. If you decide to participate, you are free to discontinue participation at any time without prejudice.

If you have any questions at a future time, Dr. Schmidt will be happy to answer them. He can be reached at (301) 295-3270.

Any information that is obtained in connection with this study and that can be identified with you will remain strictly confidential and will be disclosed only with your permission.

You are making a decision whether or not to participate. Your signature indicates that you have read the information provided above and have decided to participate. You may withdraw at any time without prejudice after signing this form should you choose to discontinue participation. You will receive a signed copy of this consent form if so desired.

_____	_____
Subject's Signature	Date
_____	_____
Witness' Signature	Investigator's Signature

Appendix N

USUHS Panic Disorder Project
Demographic Information Survey

Name: _____ Date: _____

Address: _____ Home Phone: _____
_____ Work Phone: _____
_____

Permanent Contact
Name: _____ Relation: _____

Address: _____ Home Phone: _____
_____ Work Phone: _____
_____

Referring Physician (if applicable)
Name: _____

Address: _____ Phone: _____
_____
_____

Sex: (circle) male female

Age: _____

Ethnicity:
_____ Caucasian
_____ African American
_____ Hispanic
_____ Other

Marital Status:
_____ Never Married
_____ Married
_____ Divorced
_____ Widowed

Employment Status:
_____ Employed
_____ Unemployed
_____ Student
_____ Homemaker

Have you ever received treatment for an anxiety problem? Y N
Have you ever been hospitalized for an anxiety problem? Y N

Vignette Study Protocol

General Introduction: (italics are read to subject)

You will be asked to listen to several stories, one at a time, which describe a person experiencing different situations. Each story is on a tape and repeated so that you will hear the same story twice.

Attach the physiological apparatus and make sure it is working.
Read:
This will measure heart rate and blood pressure during the experiment. You need to sit quietly for several minutes while we make sure the equipment is working properly.

After the apparatus is attached and working, have them sit for **5 minutes**. Mark on the tape the baseline period.

Hand the person the **Baseline API**. Have them complete it.
Read:
Please fill this out according to how you were feeling during the past 5 minutes.

While they are completing the form, select the tape order at random. Mark the tape order on the four **Experimental API (1, 2, 3, 4)** forms in the space provided (i.e., Tape A, Tape C, Tape B, Tape D).

After they have completed the **Baseline API**. Have them sit back.

Read:
Simply sit back in the chair, close your eyes, and listen to the first story. Try to imagine yourself, as best as you can, experiencing the same things that are going on in the story. You will complete several forms after each story.

Read the instructions below:

Introduction to the First Vignette:

The story will describe in detail the thoughts and feelings someone might experience in a situation. Allow yourself, as best as you can, to "get into the shoes" of the person being described. Try to imagine yourself feeling and thinking what they are experiencing.

Play Tape 1.

Mark the physio monitoring tape to indicate the end of the period.
Hand the person the **Experimental API (1)**.

Read:
Fill out this according to how you felt during the first tape.

Cue up the second tape while they are completing the form.

After they are finished:

Introduction to the Second Vignette:

This is another story. Remember to allow yourself, as best as you can, to "get into the shoes" of the person being described. Try to imagine yourself feeling and thinking what they are experiencing as you hear the story.

Play Tape 2.

Mark the physio monitoring tape to indicate the end of the period.
Hand the person the **Experimental API (2)**.

Read:
Fill out this according to how you felt during the tape.

Cue up the third tape while they are completing the form.

Introduction to the Third Vignette:

This is another story. Remember to allow yourself, as best as you can, to "get into the shoes" of the person being described. Try to imagine yourself feeling and thinking what they are experiencing as you hear the story.

Play Tape 3.

Mark the physio monitoring tape to indicate the end of the period.
Hand the person the **Experimental API (3)**.

Read:
Fill out this according to how you felt during the tape.

Cue up the fourth tape while they are completing the form.

After they are finished:

Introduction to the Fourth Vignette:

This is the final story. Remember to allow yourself, as best as you can, to "get into the shoes" of the person being described. Try to imagine yourself feeling and thinking what they are experiencing as you hear the story.

Play Tape 4.

Mark the physio monitoring tape to indicate the end of the period.
Hand the person the **Experimental API (4)**.

Read:
Fill out this according to how you felt during the tape.

After they are finished:

We are done with this part of the assessment.

Prepare for the next phase of the assessment.

Appendix P

Appendix A Subject Phone Screen

Hi, I am _____, a doctoral student in clinical psychology at the Uniformed Services University of the Health Sciences. I am calling to ask whether you are interested in participating in a research study. The study involves coming in for one 3-5 hour visit where you will fill out some questionnaires, be interviewed by a clinical psychology doctoral student, and complete several tasks. None of the procedures are harmful or dangerous in any way. For instance there are no needles or blood draws or taking of any drugs. For your participation, you will be compensated with a 40 dollar check. Do you think you might be interested in participating?

If "NO", say "Thank you anyway for your time. Good-bye.

If "YES", continue with the next part of the phone screen.

PHONE SCREEN INTERVIEW

Interviewer: _____ Date: _____

Name: _____

Address: _____

_____ (Include zip code)

Home Phone: _____ Work Phone: _____

Sex: M F

1. Have you ever received treatment for an anxiety disorder and/or panic attacks?

   Y N

2. Have you ever seen anyone (counselor, therapist, doctor) for any emotional or psychiatric problems?

   Y N

3. Have you ever been hospitalized for an emotional or psychiatric problem?

   Y N

4. Have you ever been hospitalized for alcohol or drug rehabilitation?

   Y N

5. Are you currently taking any psychiatric medications?

   Y N

6. Are you currently taking any other medications?

   Y N

7. Do you have any heart problems?

   Y N

PANIC STUDY PHONE SCREENING INTERVIEW

Interviewer:_____ Date: _____

1. NAME (First and Last):_____

2. ADDRESS(include city, state, zip):_____

3. HOME PHONE: _____ WORK PHONE:_____

4. SEX: M F

5. HOW DID YOU HEAR ABOUT OUR PROGRAM?

6. HAVE YOU EVER SEEN ANYONE (COUNSELOR, THERAPIST, DOCTOR) FOR ANY EMOTIONAL OR PSYCHIATRIC PROBLEMS?

IF SO, WHAT?

7. HAVE YOU EVER BEEN HOSPITALIZED FOR AN EMOTIONAL OR PSYCHIATRIC PROBLEM?

IF SO, WHAT?

8. ARE YOU CURRENTLY TAKING ANY PRESCRIPTION MEDICATIONS ?

IF YES, DESCRIBE (WHAT FOR , DOSE).

9. HAVE YOU EVER TAKEN ANY (OTHER) PRESCRIPTION MEDICATION FOR STRESS OR ANXIETY?

IF YES, DESCRIBE (WHEN, DURATION, DOSE).

10. **FEMALES**: ARE YOU CURRENTLY PREGNANT OR PLANNING TO BECOME PREGNANT WITHIN THE NEXT 12 MONTHS?

11. DO YOU CURRENTLY HAVE ANY ONE OR MORE OF THE FOLLOWING MEDICAL CONDITIONS? HEART DISEASE, ACTIVE ULCER, RENAL DISEASE, RESPIRATORY DISEASE, EPILEPSY, OR STROKE?
Describe:

ANY OTHER CONDITIONS THAT MIGHT BE SIGNIFICANTLY AFFECTING YOUR CURRENT STATE OF HEALTH?
Describe:

**********PANIC SCREEN**********

1. HAVE YOU HAD TIMES WHEN YOU FELT A SUDDEN RUSH OF INTENSE FEAR OR ANXIETY OR FEELING OF IMPENDING DOOM IN A SITUATION FOR NO APPARENT REASON?

IF YES,

1A. HAVE THESE FEELINGS ONLY OCCURRED WHEN YOU'RE IN A SITUATION THAT USUALLY MAKES YOU ANXIOUS--FOR EXAMPLE, APPLYING FOR A NEW JOB?

1B. HAVE THESE FEELING ONLY OCCURRED WHEN YOU'RE IN A SITUATION WHERE YOU ARE THE FOCUS OF OTHER PEOPLE'S ATTENTION? FOR EXAMPLE, SPEAKING IN FRONT OF A GROUP OF PEOPLE?

1C. HAVE YOU EVER HAD THESE FEELING COME "FROM OUT OF THE BLUE" THAT IS, SITUATIONS WHERE YOU DID NOT EXPECT THEM TO OCCUR?

2A. AFTER YOU HAD THESE FEELINGS (a panic attack), DID YOU WORRY ABOUT IT FOR 4 WEEKS OR MORE?

2B. AFTER YOU HAD THESE FEELINGS (a panic attack), DID YOU WORRY ABOUT HAVING MORE EPISODES FOR 4 WEEKS OR MORE?

2C. AFTER YOU HAD THESE FEELINGS (a panic attack), DID YOU CHANGE YOUR BEHAVIOR AS A RESULT OF IT FOR 4 WEEKS OR MORE?

3A. IN THE LAST MONTH, HOW MUCH HAVE YOU WORRIED ABOUT HAVING A PANIC ATTACK? (RECORD ONE FROM THE LIST BELOW).

0-NO WORRY DURING THE LAST MONTH

1-RARELY WORRIED(I.E., LESS THAN 10% OF THE DAYS)

2-OCCASIONALLY WORRIED (BETWEEN 10 AND 50% OF THE DAYS)

3-FREQUENTLY WORRIED (BETWEEN 50 AND 90% OF THE DAYS)

4-CONSTANTLY WORRIED (EVERY DAY OR ALMOST EVERY DAY)

3B. SOME PEOPLE ARE MORE FRIGHTENED BY PANIC ATTACKS THAN OTHERS. DURING THE PAST MONTH HOW WOULD YOU RATE YOURSELF IN TERMS OF YOUR FEAR OF HAVING A PANIC ATTACK?
(RECORD ONE FROM THE LIST BELOW).

0-NO FEAR AT ALL

1-MILD FEAR

2-MODERATE FEAR

3-SEVERE FEAR

4-EXTREME (VERY SEVERE) FEAR

4. NOW I'M GOING TO ASK YOU ABOUT YOUR **WORST ATTACK**.
DURING THAT ATTACK DID YOU (YES OR NO):

-FEEL SHORT OF BREATH?	Y	N
-FEEL DIZZY, UNSTEADY, OR LIKE YOU MIGHT FAINT?	Y	N
-FEEL YOUR HEART RACE, POUND, OR SKIP?	Y	N
-TREMBLE OR SHAKE?	Y	N
-SWEAT?	Y	N
-FEEL AS IF YOU WERE CHOKING?	Y	N
-HAVE NAUSEA, AN UPSET STOMACH, OR FEEL AS IF YOU WERE GOING TO HAVE DIARRHEA?	Y	N
-FEEL THAT THINGS AROUND YOU SEEMED UNREAL, OR THAT YOU FELT DETACHED FROM PART OF YOUR BODY?	Y	N
-HAVE TINGLING OR NUMBNESS IN ANY PART OF YOUR BODY?	Y	N
-HAVE HOT FLASHES OR CHILLS?	Y	N
-HAVE CHEST PAIN OR PRESSURE?	Y	N
-FEEL AFRAID THAT YOU MIGHT DIE?	Y	N
-FEEL AFRAID THAT YOU WERE GOING CRAZY OR THAT YOU MIGHT LOSE CONTROL?	Y	N
-FEEL AFRAID THAT YOU WERE GOING TO MAKE A FOOL OF YOURSELF?	Y	N
-HAVE A SWEET TASTE COME INTO YOUR MOUTH?	Y	N

5. DURING YOUR WORST ATTACK, DID THE SYMPTOMS COME ON ALL OF THE SUDDEN? (NOTE CODE YES ONLY IF THE SUBJECT EXPERIENCED THE MAJOR SYMPTOMS ALL WITHIN 10 MINUTES OF THE FIRST SYMPTOM.)
Y N

6. JUST BEFORE YOU BEGAN HAVING PANIC ATTACKS, WERE YOU TAKING ANY DRUGS, STIMULANTS, OR MEDICINES?

7. JUST BEFORE YOU BEGAN HAVING PANIC ATTACKS, WERE YOU PHYSICALLY ILL?

IF YES,

7A. SINCE THAT TIME HAVE YOU HAD AN ATTACK WHEN YOU WERE NOT ILL?

8. DURING THE PAST MONTH (30 DAYS), HOW MANY PANIC ATTACKS HAVE YOU HAD?

9. DURING THE PAST MONTH, HOW MUCH HAVE THE PANIC ATTACKS (OR FEAR OF HAVING PANIC ATTACKS) INTERFERED WITH YOUR LIFE, JOB, TRAVELING, ACTIVITIES, ETC.

(RECORD LEVEL OF INTERFERENCE FROM THE LIST BELOW)

0--NONE

1--MILD

2--MODERATE

3--SEVERE

4--VERY SEVERE/GROSSLY DISABLING

11. ARE THERE SITUATIONS OR PLACES THAT YOU NOW EITHER AVOID OR ENDURE WITH INTENSE ANXIETY BECAUSE YOU ARE AFRAID THEY MIGHT BRING ON AN ATTACK?

IF YES, ASK SUBJECT TO ELABORATE/EXPLAIN FURTHER.

PHONESCREENER MUST BE ABLE TO CHOOSE ONE OF THE FOLLOWING:

0--NO AVOIDANCE("NONE")

1--SOME AVOIDANCE, BUT RELATIVELY NORMAL LIFESTYLE ("MILD")

2--MARKED AVOIDANCE RESULTING IN CONSTRICTED LIFESTYLE ("MODERATE")

3--NEARLY OR COMPLETELY HOUSEBOUND, OR UNABLE TO LEAVE HOUSE UNACCOMPANIED ("SEVERE")

**********PSYCHOTIC SCREEN**********

1. HAS THERE EVER BEEN A PERIOD OF TIME WHEN YOU HAD STRANGE OR UNUSUAL EXPERIENCES SUCH AS:

1A. HEARING OR SEEING THINGS THAT OTHER PEOPLE DIDN'T NOTICE?

1B. VOICES OR CONVERSATIONS WHEN NO ONE ELSE WAS AROUND?

1C. VISIONS THAT NO ONE ELSE COULD SEE?

1D. HAVE YOU HAD THE FEELING THAT SOMETHING ODD WAS GOING ON AROUND YOU, THAT PEOPLE WERE DOING THINGS TO TEST YOU OR ANTAGONIZE YOU, OR HURT YOU SO THAT YOU FELT YOU HAD TO CONSTANTLY BE ON GUARD?

IF YES TO ANY OF THE ABOVE:

2. WHEN DID THIS FIRST HAPPEN?

3. DO YOU STILL EXPERIENCE THESE NOW?

COMMENTS:

****
****

DISPOSITION BASED ON PHONE SCREEN:

1- DEFINITE PANIC DISORDER

2-PROBABLE PANIC DISORDER

3-PANIC DISORDER DX UNCLEAR

4-NO CURRENT PANIC DISORDER DX